

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
17 July 2003 (17.07.2003)

PCT

(10) International Publication Number  
WO 03/057722 A2(51) International Patent Classification<sup>7</sup>: C07K 5/12,  
A61K 38/12, A61P 29/00, 35/00, 37/06

(21) International Application Number: PCT/JP02/13754

(22) International Filing Date:  
27 December 2002 (27.12.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
PR 9779 28 December 2001 (28.12.2001) AU  
2002952117 10 October 2002 (10.10.2002) AU

(71) Applicant (for all designated States except US): FUJISAWA PHARMACEUTICAL CO., LTD. [JP/JP]; 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP).

(72) Inventors; and

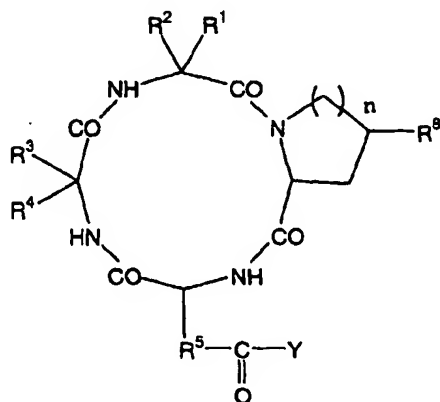
(75) Inventors/Applicants (for US only): SATOH, Shigeki [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). URANO, Yasuharu [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome,

Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). OSODA, Kazuhiko [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). HOSAKA, Mitsuru [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). SAWADA, Kozo [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). INOUE, Takayuki [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). MORI, Hiroaki [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). TAKAGAKI, Shoji [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). FUJIMURA, Takao [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). MATSUOKA, Hideaki [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). YOSHIZAWA, Katsuhiko [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP).

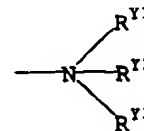
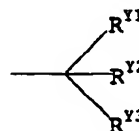
(74) Agent: TAKASHIMA, Hajime; Fujimura Yamato Seimei Bldg., 2-14, Fushimimachi 4-chome, Chuo-ku, Osaka-shi, Osaka 541-0044 (JP).

[Continued on next page]

(54) Title: CYCLIC TETRAPEPTIDE COMPOUND AND USE THEREOF



(I)



(57) Abstract: A cyclic tetrapeptide compound of the formula (I): wherein  $R_1$  is hydrogen;  $R_2$  is lower alkyl, aryl, optionally substituted ar(lower)alkyl, heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl or arylcarbamoyl(lower)alkyl;  $R_3$  and  $R_4$  are each independently hydrogen, lower alkyl, optionally substituted ar(lower)alkyl, optionally substituted heterocyclic(lower)alkyl or cyclo(lower)alkyl(lower)alkyl, or  $R_3$  and  $R_4$  are linked together to form lower alkylene or condensed ring, or one of  $R_3$  and  $R_4$  is linked to the adjacent nitrogen atom to form a ring;  $R_5$  is lower alkylene or lower alkenylene, Y is [wherein  $R_{Y1}$  is hydrogen, halogen or optionally protected hydroxy,  $R_{Y2}$  is hydrogen, halogen, lower alkyl or phenyl, and  $R_{Y3}$  is hydrogen or lower alkyl];  $R_6$  is hydrogen or lower alkyl; and n is an integer of 1 or 2, or a salt thereof.



(81) **Designated States (national):** AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished upon receipt of that report

(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

## DESCRIPTION

## CYCLIC TETRAPEPTIDE COMPOUND AND USE THEREOF

5 TECHNICAL FIELD

The present invention relates to a cyclic tetrapeptide compound which is useful as a medicament, to a process for producing the same and to a pharmaceutical composition comprising the same.

10 BACKGROUND ART

Histone deacetylases are known to play an essential role in the transcriptional machinery for regulating gene expression, and histone deacetylase inhibitors induce histone hyperacetylation and affect the gene expression. Therefore, a histone deacetylase inhibitor is useful  
15 as a therapeutic or prophylactic agent for diseases caused by abnormal gene expression, such as inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), protozoal infection, and the like.

In this connection, JP-A-7-196686 discloses a cyclic  
20 tetrapeptide compound that can be used as an antitumor agent, but this publication is silent on the action against histone deacetylases and the effect against the above-mentioned various diseases.

SUMMARY OF THE INVENTION

25 The present invention relates to a novel cyclic tetrapeptide compound which is useful as a medicament, to a process for producing the same and to a pharmaceutical composition comprising the same.

More particularly, the present invention relates to a cyclic tetrapeptide compound which has a potent inhibitory effect on the  
30 activity of histone deacetylase.

The inventors of the present invention have also found that a histone deacetylase inhibitor, such as cyclic tetrapeptide compound of formula (I) (hereinafter cyclic tetrapeptide compound [I] or compound [I]), has a potent immunosuppressive effect and potent antitumor  
35 effect. Therefore, a histone deacetylase inhibitor, such as cyclic tetrapeptide compound [I], is useful as an active ingredient of an

immunosuppressant and an antitumor agent and useful as a therapeutic or prophylactic agent for an organ transplant rejection, autoimmune diseases, tumor, and the like.

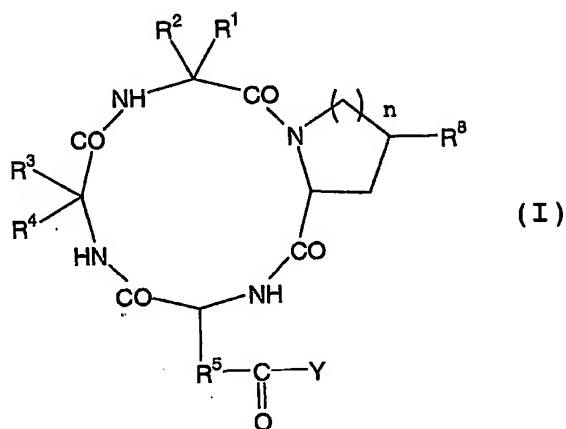
Accordingly, one object of the present invention is to provide  
5 a compound which has biological activities as stated above.

A further object of the present invention is to provide a pharmaceutical composition containing, as an active ingredient, the cyclic tetrapeptide compound [I].

A yet further object of the present invention is to provide a  
10 use of the histone deacetylase inhibitors, such as cyclic tetrapeptide compound [I], for treating and preventing diseases as stated above.

A yet further object of the present invention is to provide a commercial package comprising the pharmaceutical composition containing the cyclic tetrapeptide compound [I] and a written matter  
15 associated therewith, the written matter stating that the pharmaceutical composition may or should be used for treating or preventing diseases as stated above.

Thus, the present invention provides a cyclic tetrapeptide compound of the formula (I):



20 wherein

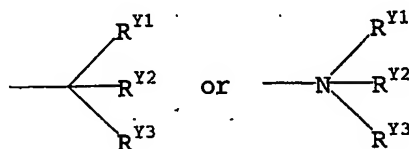
R<sup>1</sup> is hydrogen,

R<sup>2</sup> is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl or

25 arylcarbamoyl(lower)alkyl,

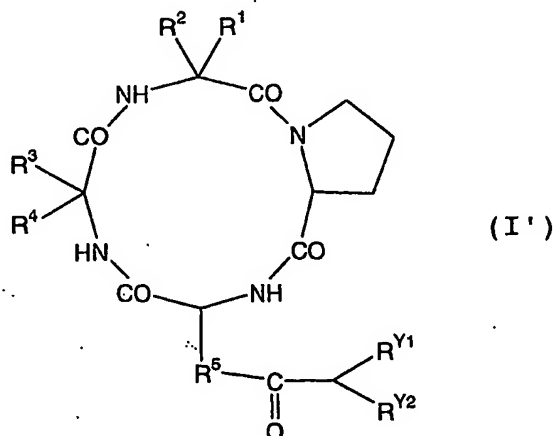
R<sup>3</sup> and R<sup>4</sup> are each independently hydrogen, lower alkyl, ar(lower)alkyl

- optionally substituted with one or more suitable substituent(s),  
 heterocyclic(lower)alkyl optionally substituted with one or more  
 suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or  
 $R^3$  and  $R^4$  are linked together to form lower alkylene or condensed ring,  
 5 or one of  $R^3$  and  $R^4$  is linked to the adjacent nitrogen atom to form a  
 ring,  
 $R^5$  is lower alkylene or lower alkenylene,  
 $Y$  is



- 10 [wherein  $R^{Y1}$  is hydrogen, halogen or optionally protected hydroxy,  
 $R^{Y2}$  is hydrogen, halogen, lower alkyl or phenyl, and  
 $R^{Y3}$  is hydrogen or lower alkyl],  
 $R^8$  is hydrogen or lower alkyl, and  
 $n$  is an integer of 1 or 2,  
 15 providing that,  
 when  $R^3$  is methyl,  $R^4$  is methyl or ethyl,  $R^5$  is pentylene,  $R^8$  is  
 hydrogen,  $n$  is 1,  $R^{Y1}$  is optionally substituted hydroxy,  $R^{Y2}$  is methyl  
 and  $R^{Y3}$  is hydrogen, then  $R^2$  is not unsubstituted benzyl,  
 or a salt thereof.

- 20 The present invention also provides a cyclic tetrapeptide  
 compound of the formula (I'):  
 wherein



- $R^1$  is hydrogen,  
 $R^2$  is ar(lower)alkyl optionally substituted with one or more suitable

substituent(s),  
R<sup>3</sup> and R<sup>4</sup> are each hydrogen or lower alkyl, or  
R<sup>3</sup> and R<sup>4</sup> are linked together to form lower alkylene,  
R<sup>5</sup> is lower alkylene or lower alkenylene,  
5 R<sup>Y1</sup> is optionally protected hydroxy, and  
R<sup>Y2</sup> is lower alkyl,  
providing that,  
when R<sup>3</sup> is methyl, R<sup>4</sup> is methyl or ethyl, R<sup>5</sup> is pentylene, R<sup>Y1</sup> is  
optionally substituted hydroxy and R<sup>Y2</sup> is methyl, then R<sup>2</sup> is not  
10 unsubstituted benzyl,  
or a salt thereof.

#### BRIEF DESCRIPTION OF THE DRAWINGS

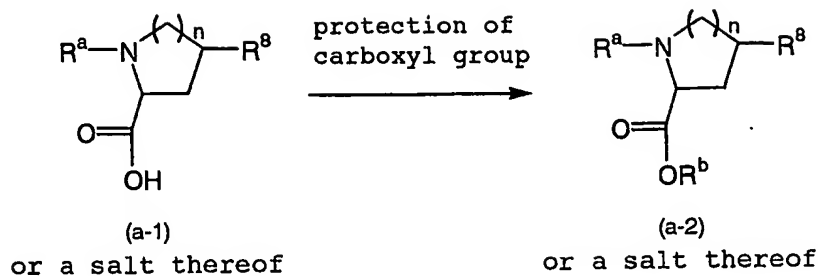
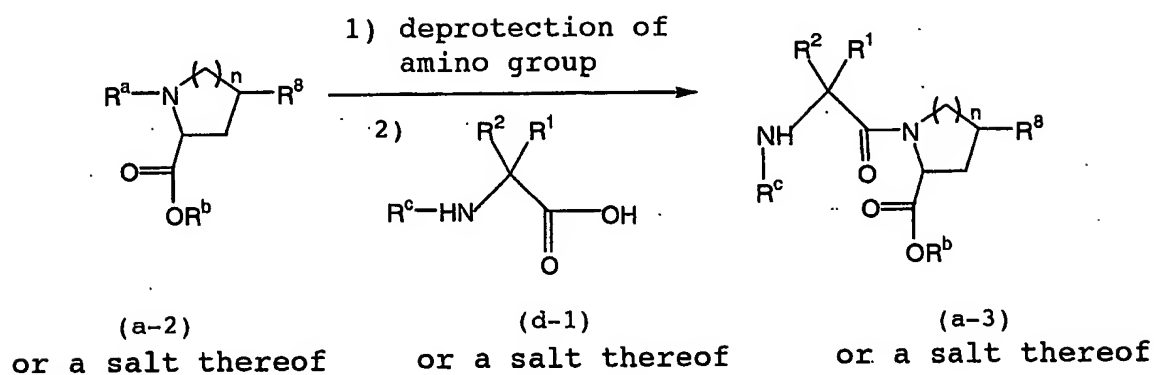
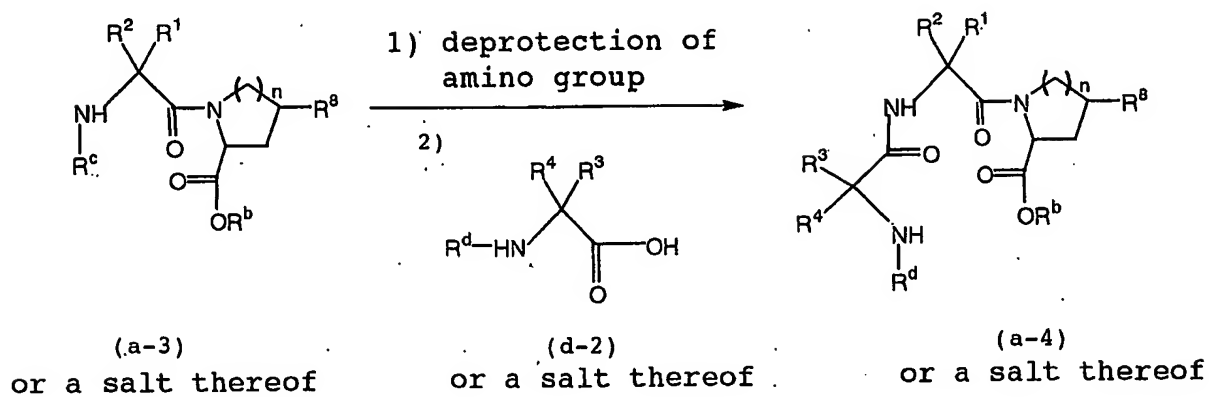
Fig.1 represents pNFkB-TA-Luc.  
15 Fig.2 represents a chart which shows the effect of the compound  
of the present invention on NF-kB activation in TNF $\alpha$ -stimulated HEL  
cells (NF-kB reporter gene assay) in comparison with the effect of  
FK506.  
Fig.3 represents a chart which shows the effect of the compound  
20 of the present invention on the MCP-1 production by activated THP-1  
cells (MCP-1 ELISA) in comparison with the effect of FK506.

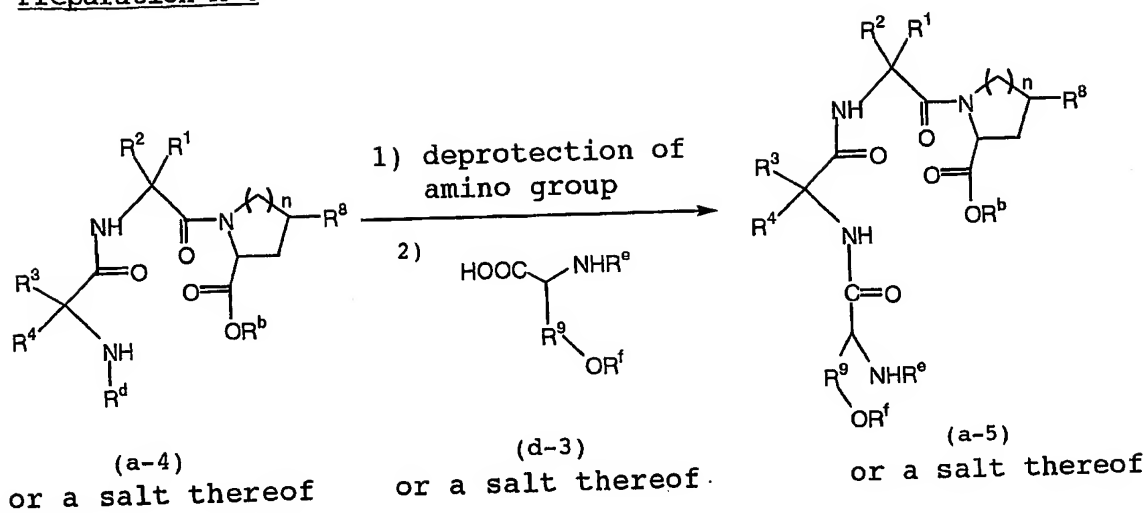
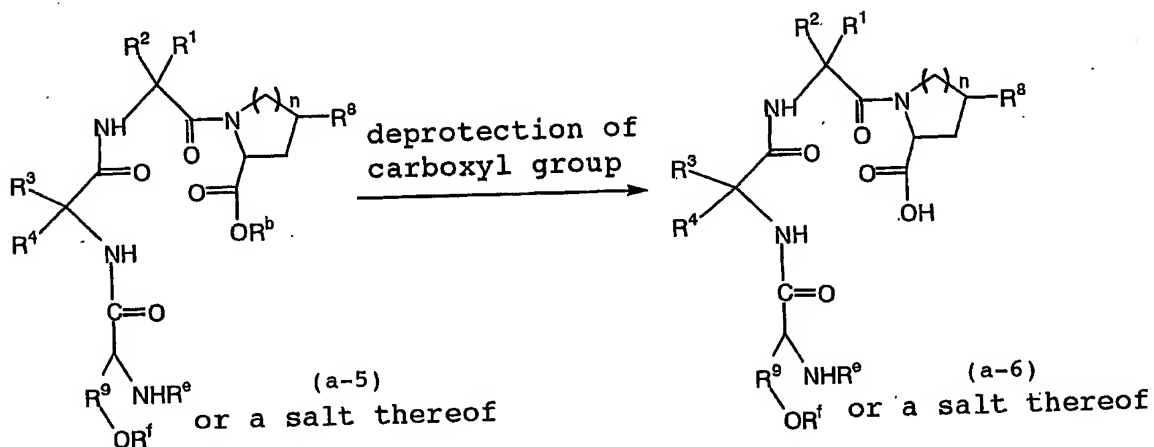
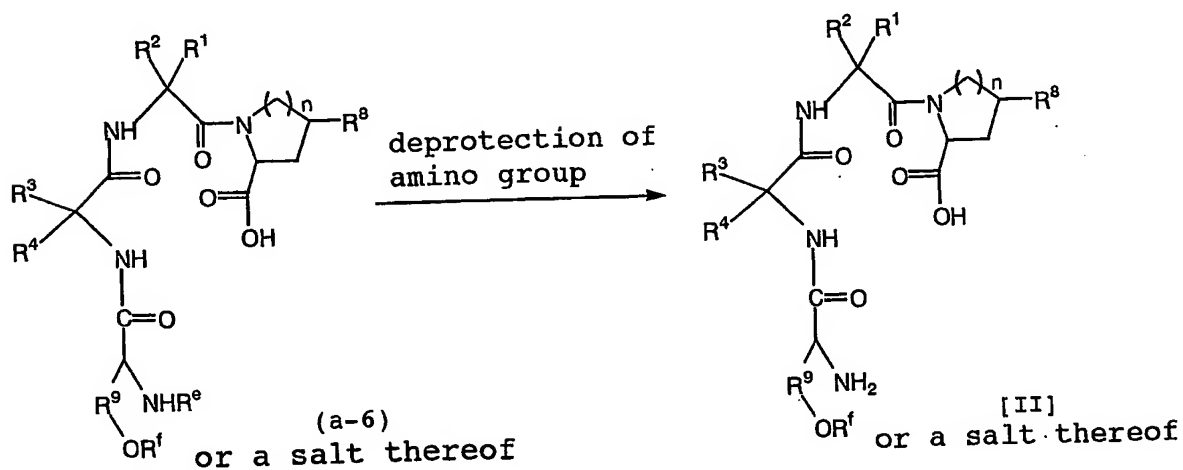
#### PREFERRED EMBODIMENT FOR CARRYING OUT THE INVENTION

The compound [I] and a salt thereof can be prepared by the  
25 process as illustrated in the following reaction schemes.

The compound [I] of the present invention may be prepared by a  
liquid phase method (i.e. Preparation A  $\rightarrow$  Preparation C  $\rightarrow$  Examples)  
or a solid phase-liquid phase relay method (i.e. Preparation B  $\rightarrow$   
Preparation C  $\rightarrow$  Examples).

30 Hereinafter, the processes for preparing the compound [I] of  
the present invention are explained in detail.

Preparation APreparation A-1Preparation A-2Preparation A-3

Preparation A-4Preparation A-55 Preparation A-6

wherein

$R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^8$  and  $n$  are as defined above,

$R^9$  is lower alkylene,

$R^a$  is hydrogen or amino protective group,

5  $R^b$  is carboxy protective group,

$R^c$ ,  $R^d$  and  $R^e$  are each independently amino protective group, and

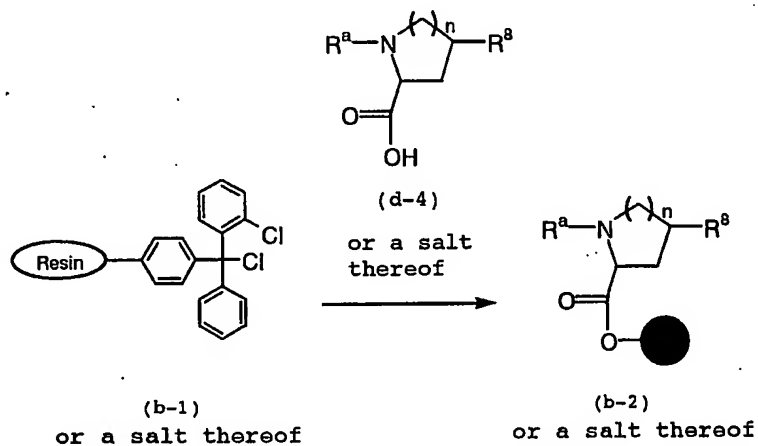
$R^f$  is hydroxy protective group.

In the above Preparation A, the deprotection of carboxyl group is exemplified by Preparation 17 and the like, and the deprotection of  
10 amino group is exemplified by Preparation 18 and the like.

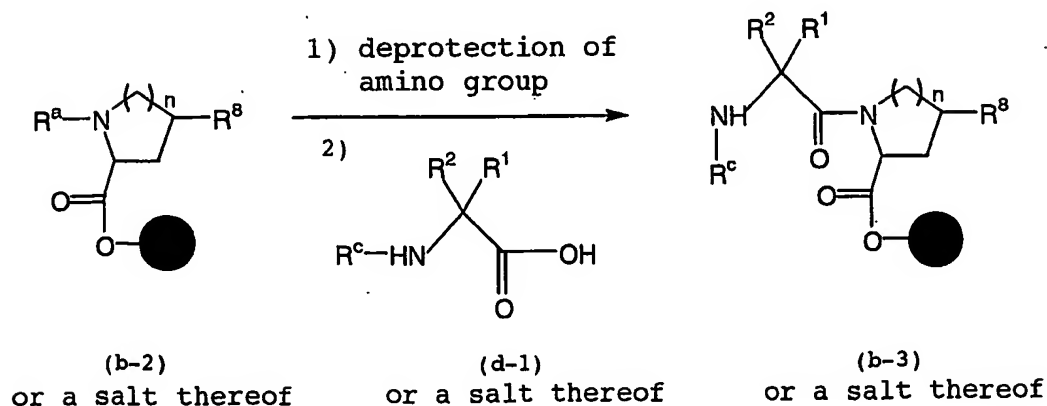
Alternatively, the deprotection of carboxyl and amino groups may be conducted simultaneously (e.g. Preparation 53; Preparation 57 and the like).

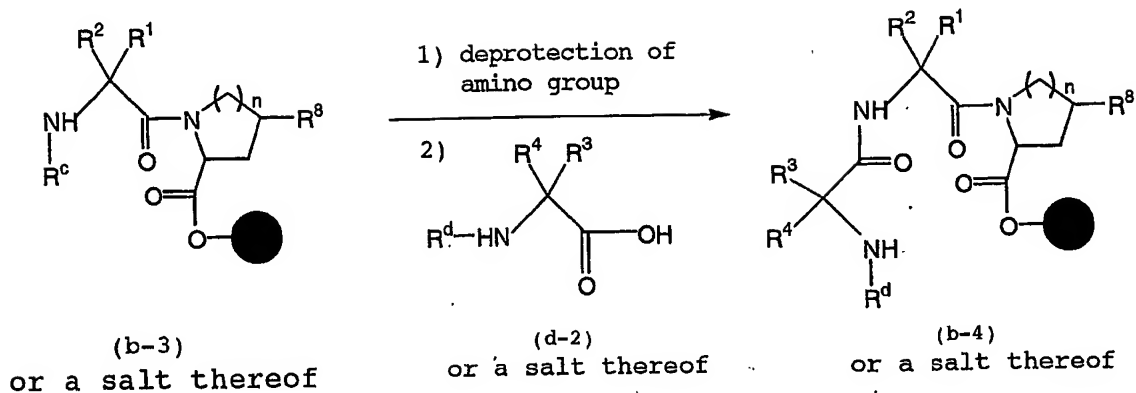
#### Preparation B

15 Preparation B-1

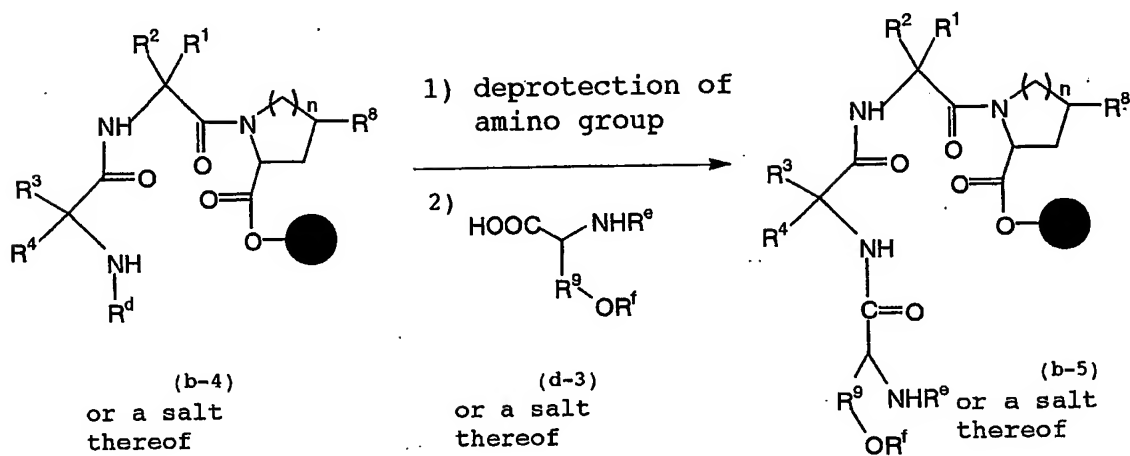
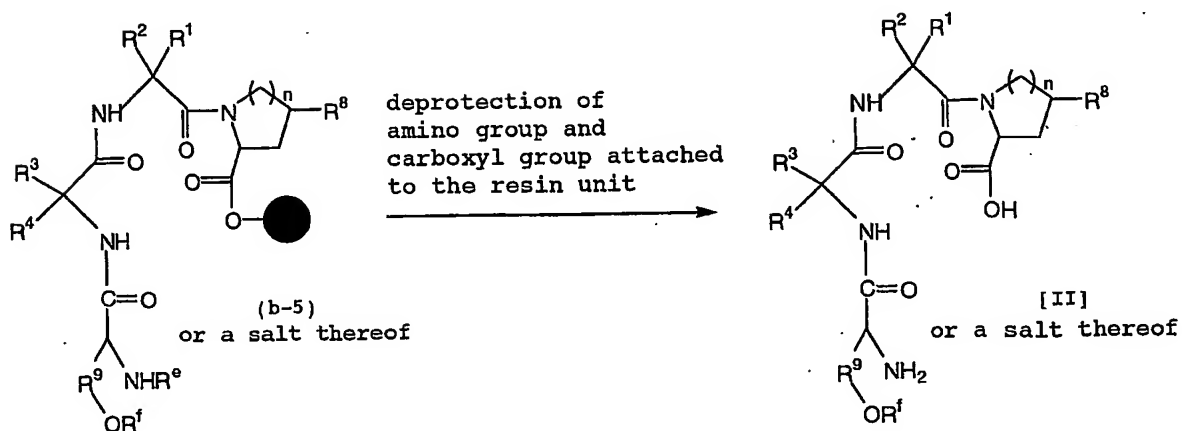


#### Preparation B-2



Preparation B-3Preparation B-4

5

Preparation B-5

wherein

$R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^8$  and  $n$  are as defined above,

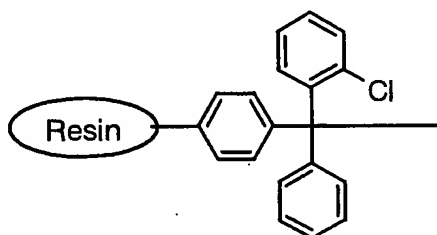
$R^9$  is lower alkylene,

$R^a$  is hydrogen or amino protective group,

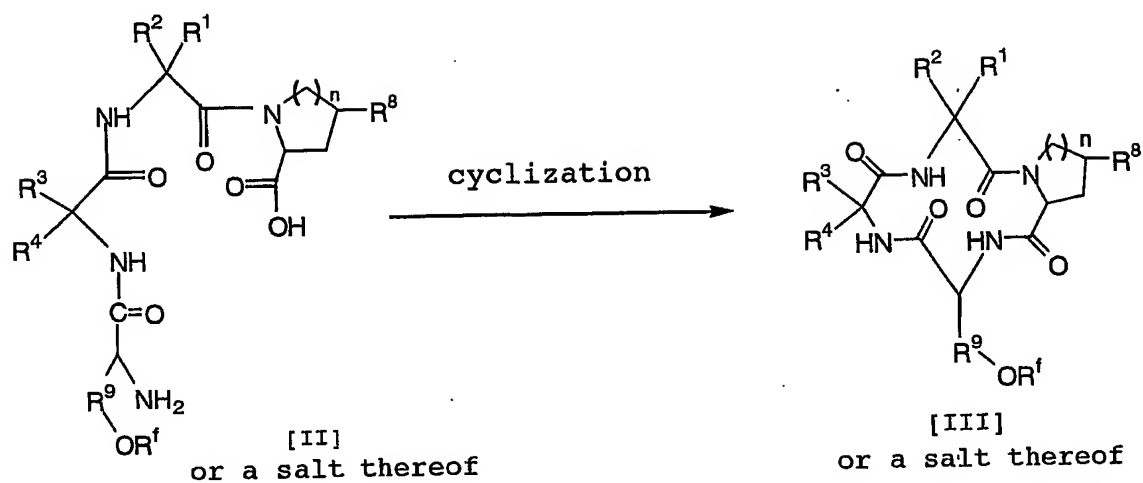
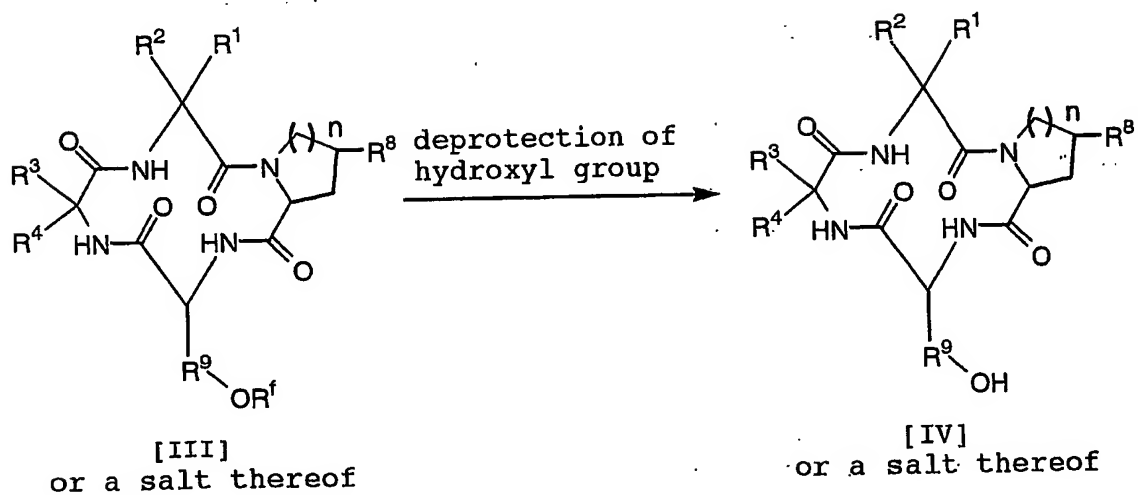
5  $R^c$ ,  $R^d$  and  $R^e$  are each independently amino protective group,

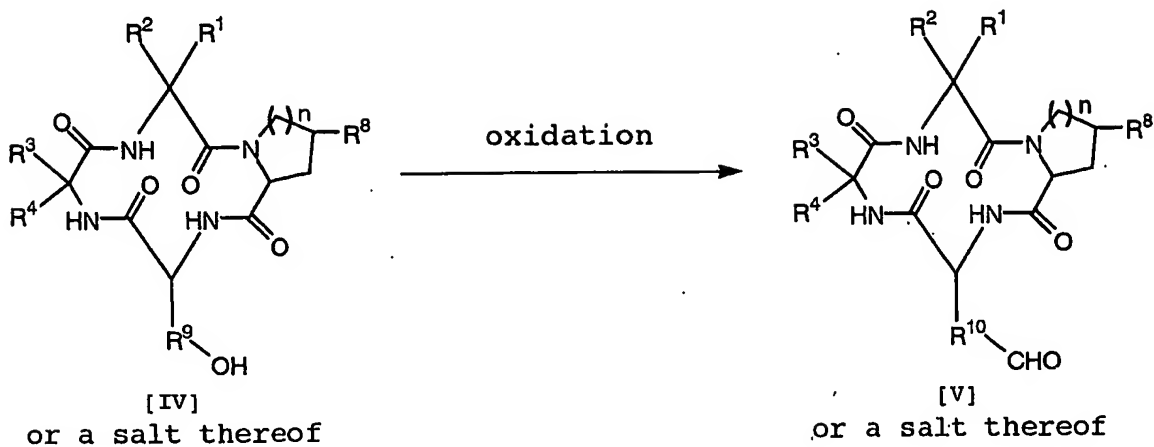
$R^f$  is hydroxy protective group, and

is the following resin unit:



wherein Resin is a resin.

Preparation CPreparation C-15 Preparation C-2

Preparation C-3

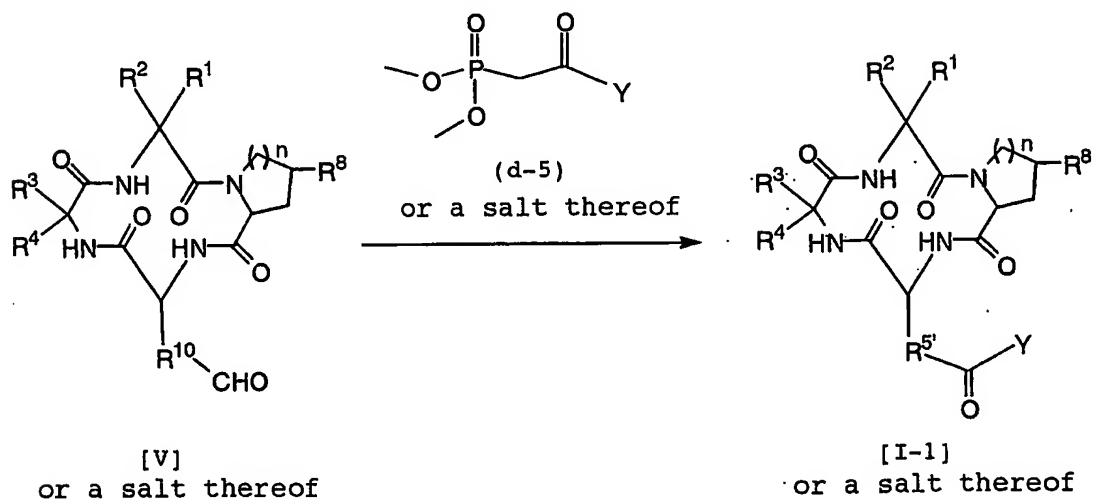
wherein

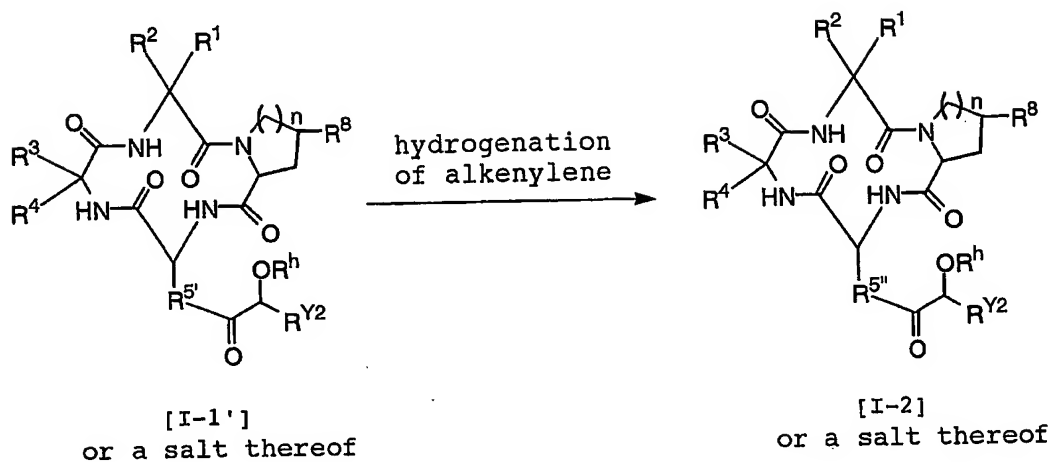
$R^1, R^2, R^3, R^4, R^8$  and  $n$  are as defined above,

- 5  $R^9$  and  $R^{10}$  are each independently lower alkylene, and  
 $R^f$  is a hydroxy protective group.

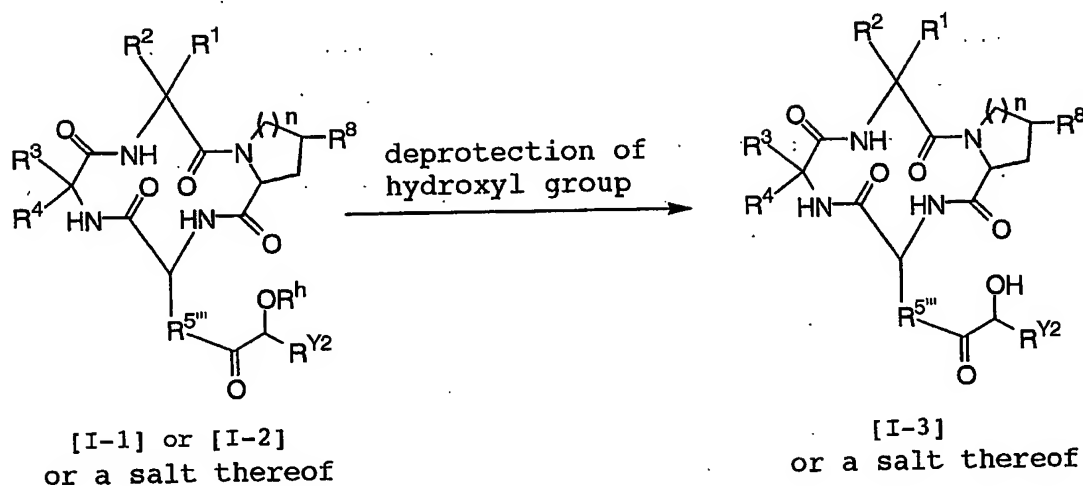
The compound [V] obtained from the Preparation C is used in the preparation of the compound [I] of the present invention.

- 10 Preparation of the compound [I] of the present invention  
Preparation of the compound [I-1]



Preparation of the compound [I-2]Preparation of the compound [I-3]

5



wherein

 $R^1, R^2, R^3, R^4, R^{Y2}, R^8, R^9$  and  $n$  are as defined above, $R^{5'}$  is lower alkenylene,10  $R^{5''}$  is lower alkylene, $R^{5'''}$  is lower alkylene or lower alkenylene, and $R^h$  is hydroxy protective group.

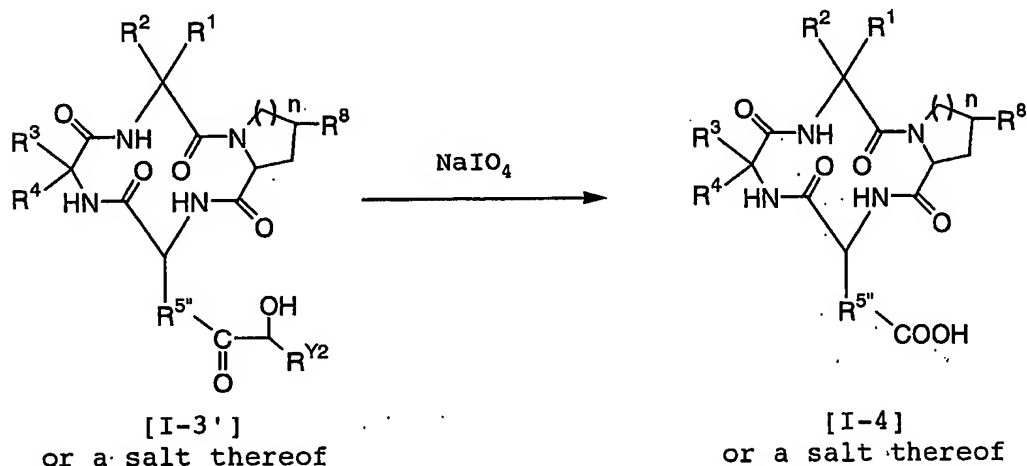
To determine absolute configuration of the hydroxyl group of the compound [I-3] and to estimate optical purity of the isomer of the

15 compound [I-3], the compound [I-3] is reacted with a reagent such as

(R or S)-(+ or -)- $\alpha$ -methoxy- $\alpha$ -trifluoromethyl- $\alpha$ -phenylacetyl chloride, 1-naphthylmethoxyacetic acid, 2-naphthylmethoxyacetic acid, 9-anthrylmethoxyacetic acid, 2-anthrylmethoxyacetic acid, and the like. This reaction is exemplified by Example 53.

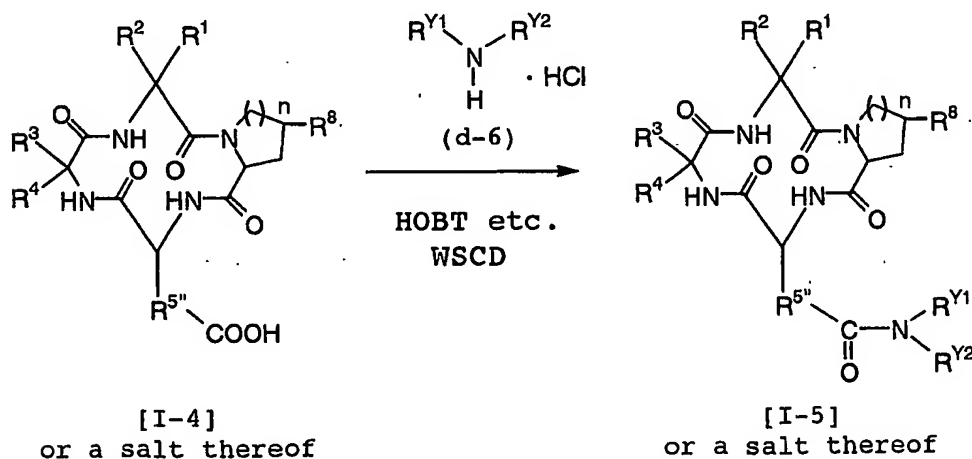
- 5 The hydroxy group of the compound [I-3] is, if desired, optionally protected with a suitable hydroxy protective group. The protection of the hydroxy group is exemplified by Examples 162, 205, 206, 207 and the like.

Preparation of the compound [I-4]

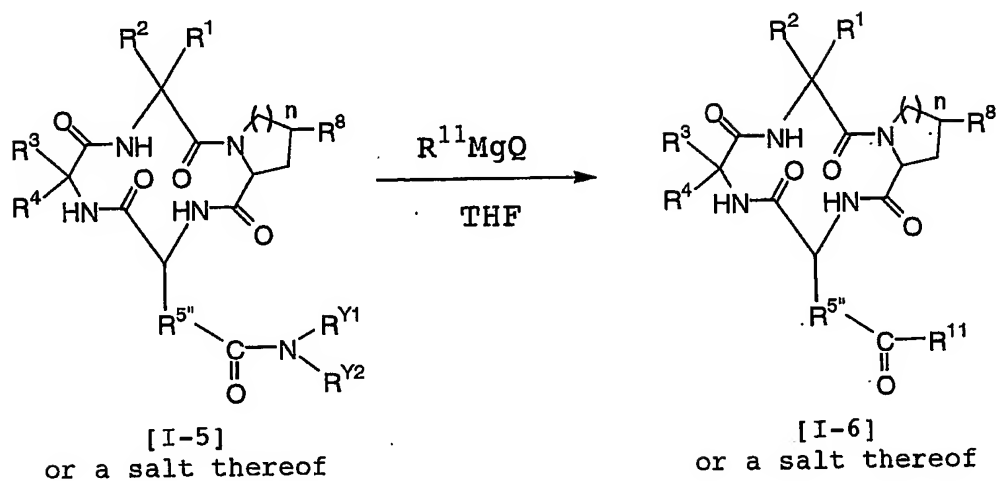
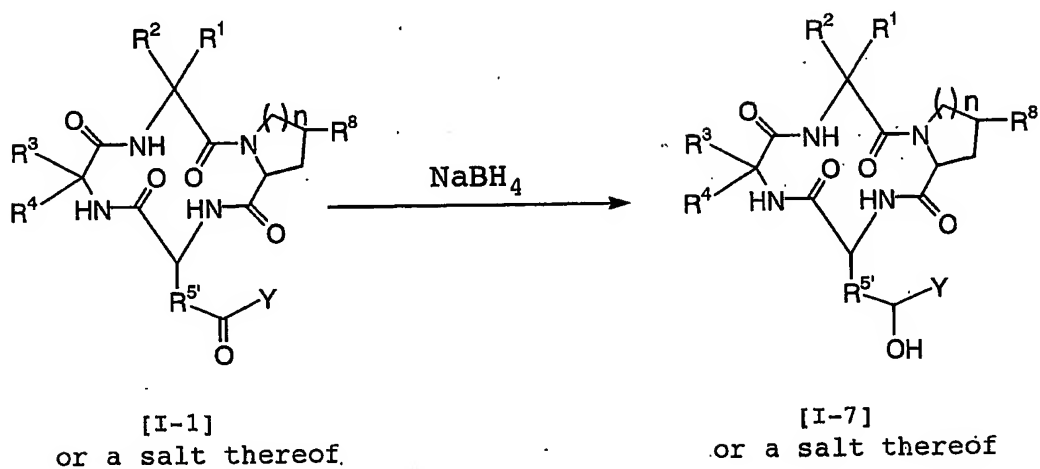


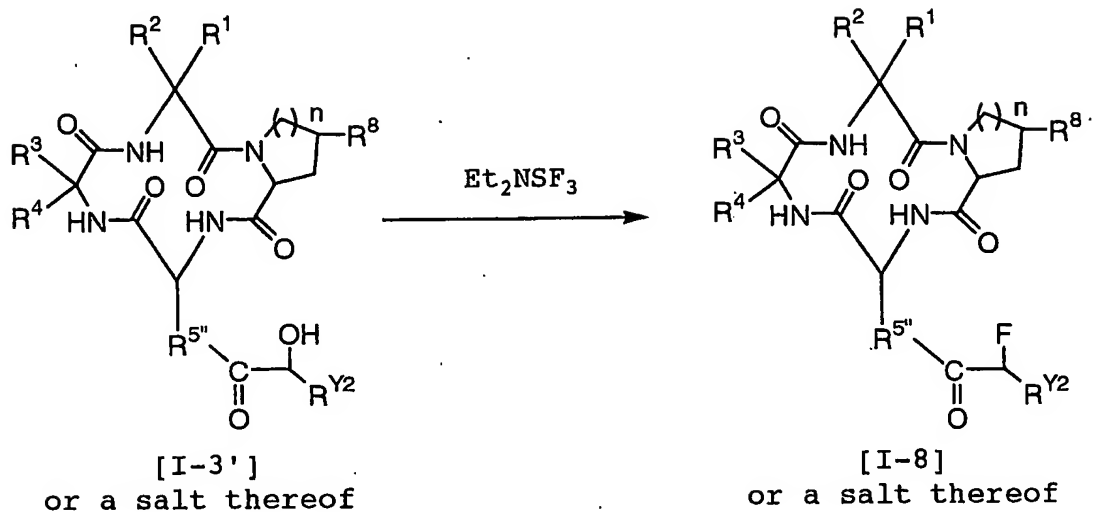
10

Preparation of the compound [I-5]

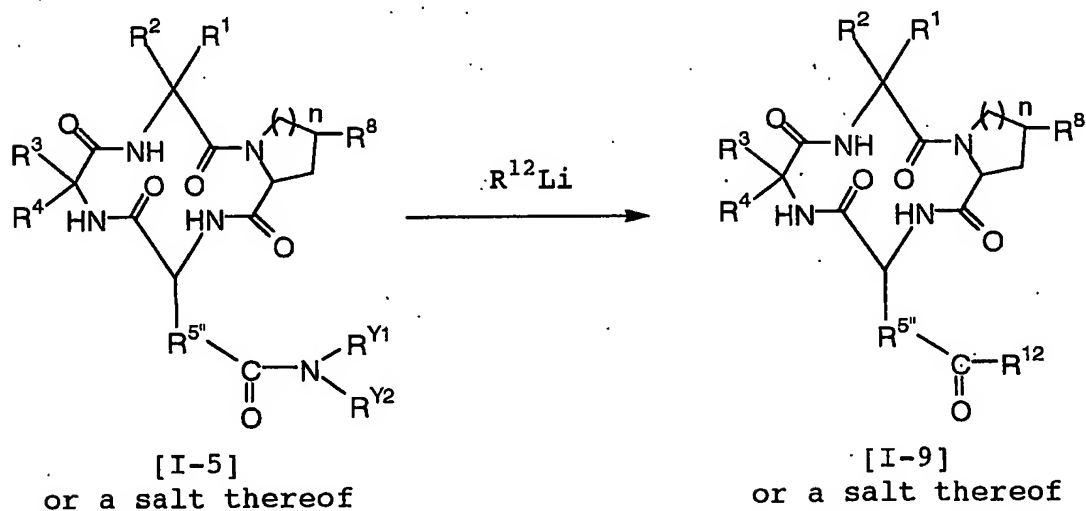


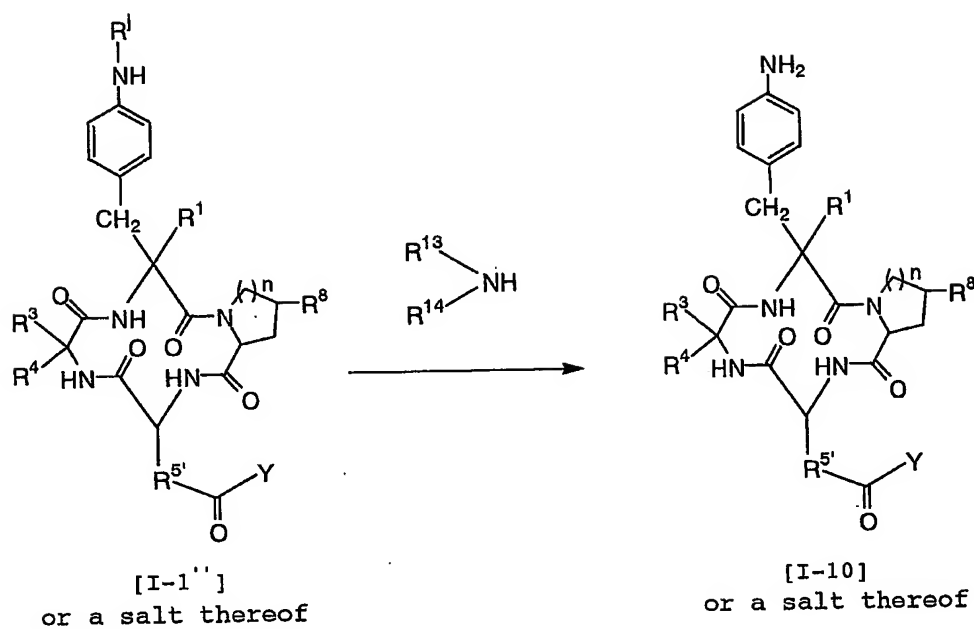
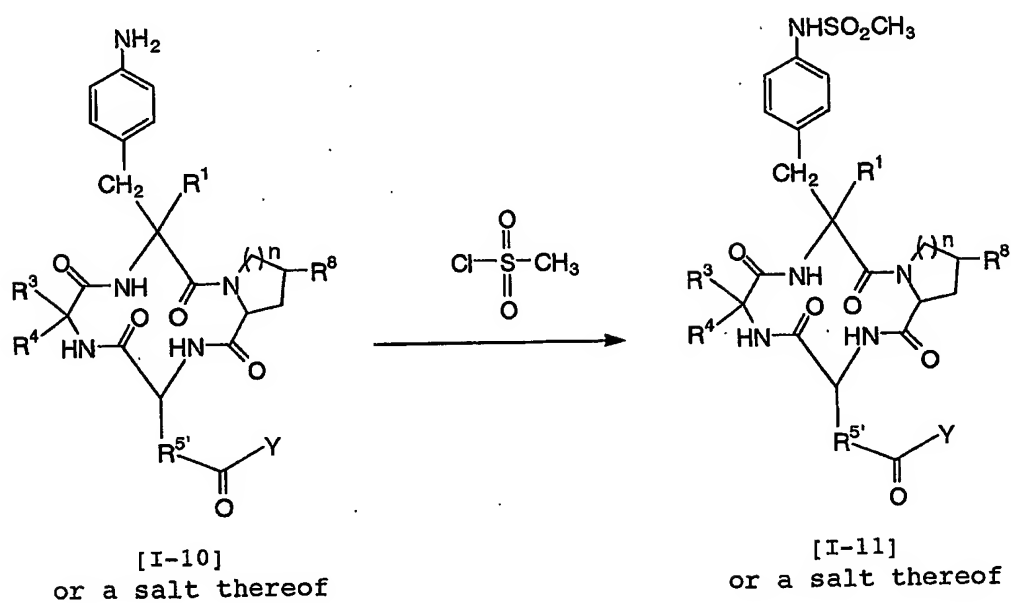
15

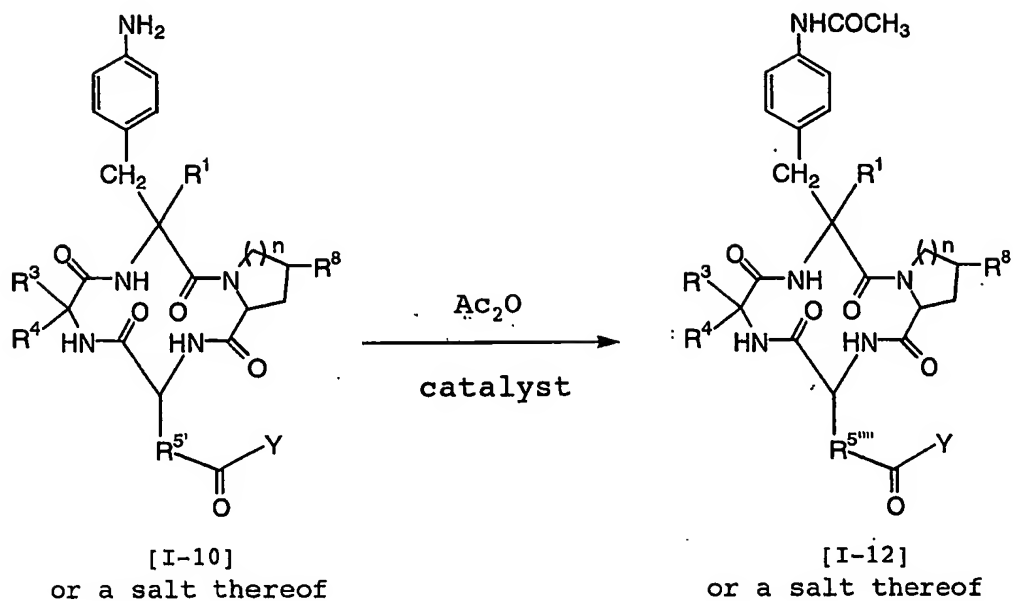
Preparation of the compound [I-6]5 Preparation of the compound [I-7]

Preparation of the compound [I-8]

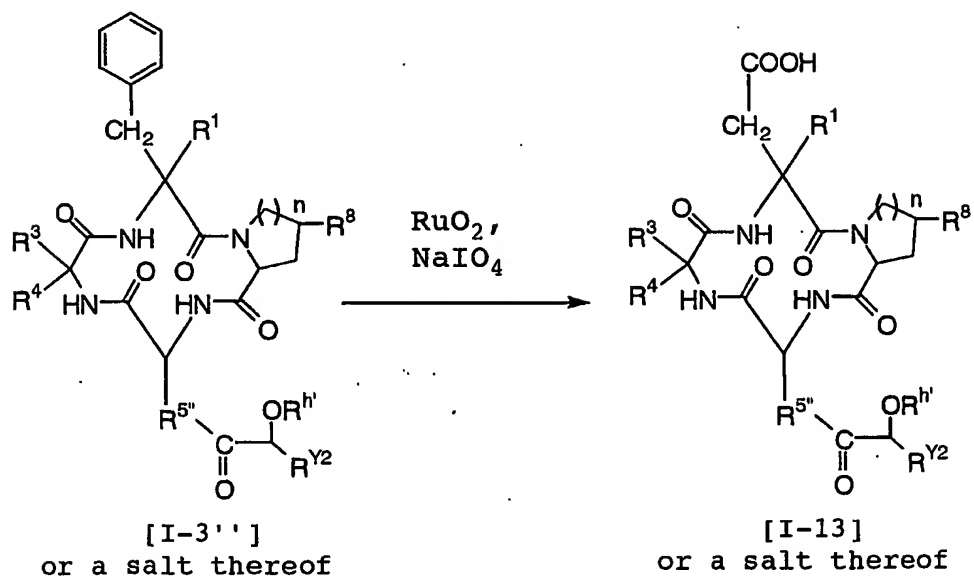
5

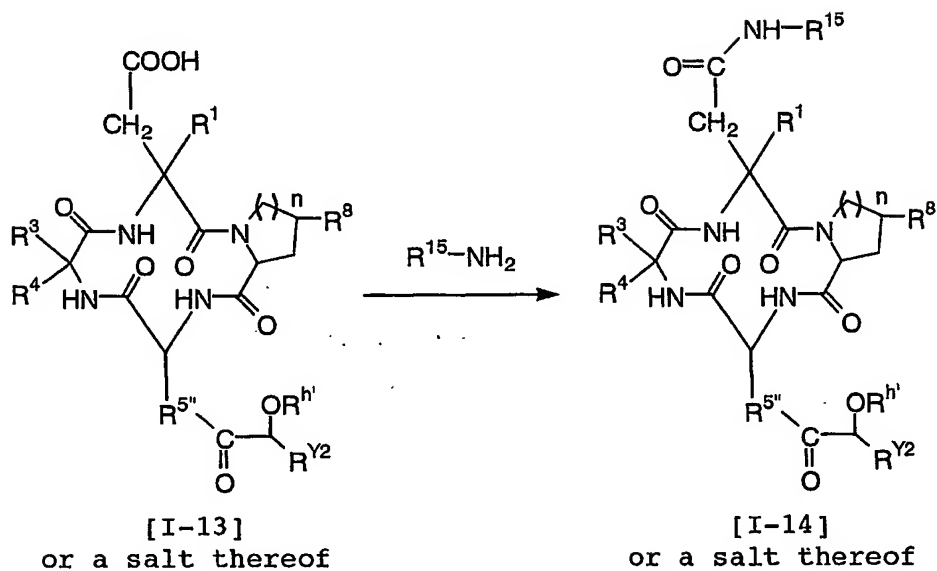
Preparation of the compound [I-9]

Preparation of the compound [I-10]Preparation of the compound [I-11]

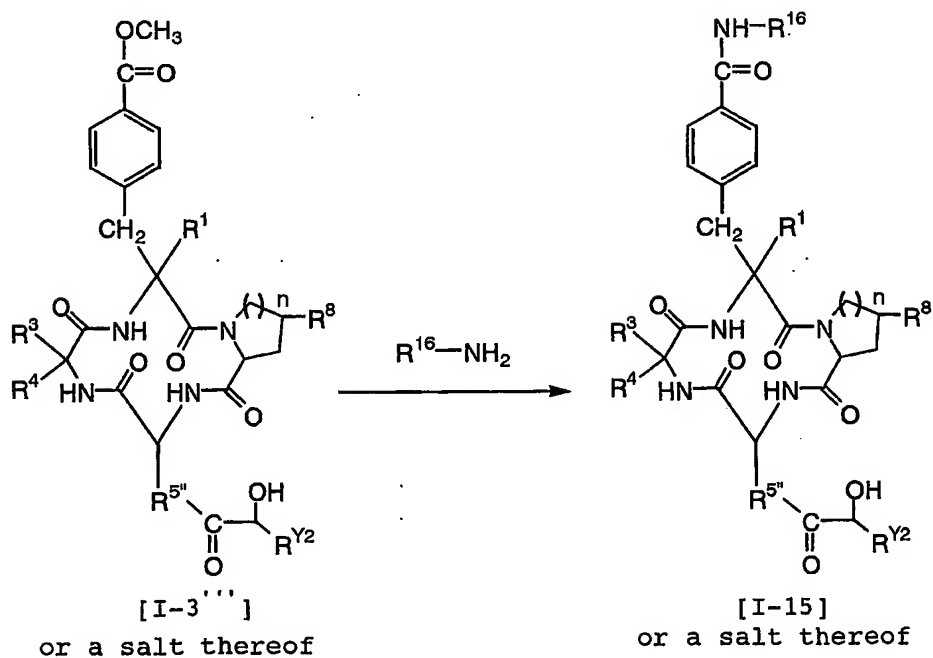
Preparation of the Compound [I-12]Preparation of the Compound [I-13]

5



Preparation of the Compound [I-14]Preparation of the Compound [I-15]

5



wherein

R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5'</sup>, R<sup>5''</sup>, R<sup>5'''</sup>, R<sup>Y1</sup>, R<sup>Y2</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, Y and n are as defined above,

10 R<sup>11</sup> is lower alkyl, aryl or ar(lower)alkyl,

- R<sup>12</sup> is lower alkyl, lower alkenyl or aryl and the like,  
R<sup>13</sup> and R<sup>14</sup> are each independently lower alkyl or lower cycloalkyl, or  
R<sup>13</sup> and R<sup>14</sup> are linked together with the adjacent nitrogen atom to form  
a ring wherein one or more methylene(s) of the ring is(are) optionally  
5 replaced by heteroatom(s) selected from an oxygen atom, a nitrogen  
atom and a sulfur atom,  
R<sup>15</sup> is lower alkyl,  
R<sup>16</sup> is lower alkyl,  
Q is halogen,  
10 R<sup>h</sup> is hydroxy protective group, and  
R<sup>j</sup> is amino protective group.

- Suitable "salt" is a pharmaceutically acceptable and  
conventional non-toxic salt, and may include a salt with a base or an  
acid addition salt such as a salt with an inorganic base, for example,  
15 an alkaline metal salt (e.g., sodium salt, potassium salt, and the  
like), an alkaline earth metal salt (e.g., calcium salt, magnesium  
salt, and the like), an ammonium salt;  
a salt with an organic base, for example, an organic amine salt (e.g.,  
triethylamine salt, diisopropylethylamine salt, pyridine salt,  
20 picoline salt, ethanolamine salt, triethanolamine salt,  
dicyclohexylamine salt, N, N'-dibenzylethylenediamine salt, and the  
like);  
an inorganic acid addition salt (e.g., hydrochloride, hydrobromide,  
sulfate, phosphate, and the like);  
25 an organic carboxylic sulfonic acid addition salt (e.g., formate,  
acetate, trifluoroacetate, maleate, tartrate, fumarate,  
methanesulfonate, benzenesulfonate, toluenesulfonate, and the like);  
and  
a salt with a basic or acidic amino acid (e.g., arginine, aspartic  
30 acid, glutamic acid, and the like).

Suitable examples and illustration of the various definitions  
in the above and subsequent descriptions, which the present invention  
intends to be included within the scope thereof, are explained in  
detail as follows:

- 35 The term "halogen" means fluorine, chlorine, bromine, and  
iodine.

The term "lower" used in the description is intended to mean 1 to 6 carbon atoms, unless otherwise indicated.

Suitable example of "one or more" may be the number of 1 to 6, preferably 1 to 3.

5        Suitable examples of "lower alkyl" may include straight or branched one having 1 to 6 carbon atom(s), such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, tert-pentyl, neopentyl, hexyl, isohexyl and the like. The preferred lower alkyl for R<sup>2</sup> may be 2-methyl-1-propyl, the preferred lower alkyl  
10    for R<sup>3</sup> and R<sup>4</sup> may be methyl, ethyl and isopropyl, the preferred lower alkyl for R<sup>Y2</sup> may be methyl and ethyl, the preferred lower alkyl for R<sup>Y3</sup> may be methyl and the preferred lower alkyl for R<sup>6</sup> may be methyl.

      Suitable examples of "lower alkylene" may include straight or branched one having 1 to 6 carbon atom(s), such as methylene, ethylene,  
15    trimethylene, propylene, tetramethylene, pentamethylene, hexamethylene and the like. The preferred lower alkylene for R<sup>3</sup> and R<sup>4</sup> may be tetramethylene, and the preferred lower alkylene for R<sup>5</sup> may be pentamethylene.

      Suitable examples of "lower alkenylene" may include straight or branched one having 1 to 6 carbon atom(s), such as ethenylene, 1-  
20    propenylene, 2-propenylene, 2-methyl-1-propenylene, 2-methyl-2-propenylene, 1-butenylene, 2-butenylene, 3-butenylene, 1-pentenylene, 2-pentenylene, 3-pentenylene, 4-pentenylene, 1-hexenylene, 2-  
25    hexenylene, 3-hexenylene, 4-hexenylene, 5-hexenylene and the like, in which the preferred one for R<sup>5</sup> may be 1-pentenylene.

      Suitable examples of "aryl" may include C<sub>6</sub>-C<sub>16</sub> aryl such as phenyl, naphthyl, anthryl, pyrenyl, phenanthryl, azulenyl and the like, preferably phenyl, naphthyl. The preferred one for R<sup>2</sup> may be phenyl, and the preferred one for Y may be phenyl.

30        Suitable examples of ar(lower)alkyl for R<sup>2</sup> may include phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl such as benzyl, phenethyl, phenylpropyl, phenylbutyl, phenylhexyl and the like, naphthyl(C<sub>1</sub>-C<sub>6</sub>)alkyl such as naphthylmethyl, naphthylethyl, naphthylpropyl, naphthylbutyl, naphthylpentyl, naphthylhexyl and the like. The preferred one for R<sup>2</sup> may be phenyl(C<sub>1</sub>-  
35    C<sub>6</sub>)alkyl, more preferably benzyl.

      Suitable examples of "suitable substituent(s)" of

"ar(lower)alkyl optionally substituted with one or more suitable substituent(s)" for R<sup>2</sup> may include lower alkyl (e.g. methyl and the like), halo(lower)alkyl (e.g. trifluoromethyl and the like) lower alkoxy (e.g. methoxy, ethoxy and the like), ar(lower)alkoxy (e.g. phenyl(lower)alkoxy and the like), cyano, hydroxy, halogen (e.g. chloro, fluoro and the like), amino, lower alkanoylamino (e.g. acetylamino and the like), lower alkylsulfonylamino (e.g. methanesulfonylamino and the like), aryl (e.g. phenyl and the like), cyclo(lower)alkyloxy (e.g. cyclopentyloxy and the like), carboxy(lower)alkoxy (e.g. carboxymethoxy and the like), heterocyclic(lower)alkoxy (e.g. pyridyl(lower)alkoxy such as pyridylmethoxy and the like), lower alkenyloxy (e.g. ethenyloxy and the like), hydroxy(lower)alkyl (e.g. hydroxymethyl and the like), arylcarbamoyle (e.g. phenylcarbamoyle and the like), heterocycliccarbonyl (e.g. piperidinocarbonyl and the like), lower(alkyl)carbamoyle(lower)alkoxy (e.g. n-pentylcarbamoylemethoxy and the like), arylcarbamoyle(lower)alkoxy (e.g. phenylcarbamoyle(lower)alkoxy such as phenylcarbamoylemethoxy and the like), lower(alkyl)carbamoyle(lower)alkyl (e.g. 2-(t-butylcarbamoyle)-1-ethyl and the like), heterocyclic group (e.g. pyridyl and the like), lower alkoxy carbonyl (e.g. methoxy carbonyl and the like), lower alkoxy carbonyl(lower)alkoxy (e.g. methoxy carbonylmethoxy and the like), lower alkylcarbamoyle (e.g. methylcarbamoyle and the like), heterocycliccarbonyl(lower)alkyl (e.g. morpholinocarbonyl(lower)alkyl such as 2-morpholinocarbonyl-1-ethyl and the like), heterocycliccarbonyl(lower)alkoxy (e.g. piperidinocarbonyl(lower)alkoxy such as piperidinocarbonylmethoxy and the like), aryl(lower)alkoxy (e.g. phenyl(lower)alkoxy such as phenylmethoxy and the like) and arylcarbamoyle(lower)alkyl (e.g. phenylcarbamoyle(lower)alkyl such as phenylcarbamoylemethyl and the like) and the like.

Suitable "heterocyclic" in the terms of "heterocyclic(lower)alkyl" for R<sup>2</sup> may include 5- or 6-membered heteromonocyclic group or condensed heterocyclic group, each of which contains at least one heteroatom(s) selected from a sulfur atom, an oxygen atom and a nitrogen atom.

Suitable 5- or 6-membered heteromonocyclic group containing at least one heteroatom(s) selected from a sulfur atom, an oxygen atom and a nitrogen atom include, for example, pyridyl, dihydropyridyl, azepinyl (e.g., 1H-azepinyl and the like), pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl (e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl and the like), tetrazolyl (e.g., 1H-tetrazolyl, 2H-tetrazolyl and the like), perhydroazepinyl (e.g., perhydro-1H-azepinyl and the like), pyrrolidinyl, imidazolidinyl, piperidyl, piperadinyl, oxazolyl, isoxazolyl, oxadiazolyl (e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl and the like), morpholinyl, sydnonyl, thiazolyl, isothiazolyl, thiadiazolyl (e.g., 1,2,3-thiazidiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl and the like), dihydrothiazinyl, thiazolidinyl, furyl, dihydrooxatiinyl and the like.

Suitable condensed heterocyclic group containing at least one heteroatom(s) selected from a sulfur atom, an oxygen atom and a nitrogen atom include, for example, indolyl, isoindolyl, indolidinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, quinoxalinyl, imidazopyridyl (e.g., imidazo[4,5-c]pyridyl and the like), tetrahydroimidazopyridyl (e.g., 4,5,6,7-tetrahydro[4,5-c]pyridyl and the like), 7-azabicyclo[2.2.1]heptyl, 3-azabicyclo[3.2.2]nonanyl, benzoxazolyl, benzoxadiazolyl, benzothiazolyl, benzothiadiazolyl, benzothienyl, benzodithiinyl, benzoxathiinyl and the like.

Among these, the preferable "heterocyclic" in the terms of "heterocyclic(lower)alkyl" for R<sup>2</sup> include, for example, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, thienyl, furyl, quinolyl, imidazolyl, indolyl and the like. The preferred "heterocyclic(lower)alkyl" for R<sup>2</sup> may be 2-pyridylmethyl, 4-pyridylmethyl, 3-indolylmethyl and the like.

Suitable "cyclo(lower)alkyl" moiety in the terms of "cyclo(lower)alkyl(lower)alkyl" for R<sup>2</sup> may be cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like. The preferred "cyclo(lower)alkyl(lower)alkyl" for R<sup>2</sup> may be cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, cyclopropylethyl, cyclobutylethyl, cyclopentylethyl, cyclohexylethyl

and the like.

Suitable example of "lower alkylcarbamoyl(lower)alkyl" for R<sup>2</sup> may include n-pentylcarbamoylmethyl and the like.

5     Suitable example of "arylcarbamoyl(lower)alkyl" for R<sup>2</sup> may include phenylcarbamoylmethyl and the like.

       Suitable "ar(lower)alkyl" for R<sup>3</sup> and R<sup>4</sup> may include phenyl(lower)alkyl [e.g. phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl such as benzyl, phenethyl, phenylpropyl, phenylbutyl, phenylhexyl and the like], naphthyl(lower)alkyl [e.g. naphthyl(C<sub>1</sub>-C<sub>6</sub>)alkyl such as naphthylmethyl, 10 naphthylethyl, naphthylpropyl, naphthylbutyl, naphthylhexyl and the like], and the like. The preferred one for R<sup>3</sup> and R<sup>4</sup> may be phenyl(C<sub>1</sub>-C<sub>6</sub>)alkyl, more preferably benzyl.

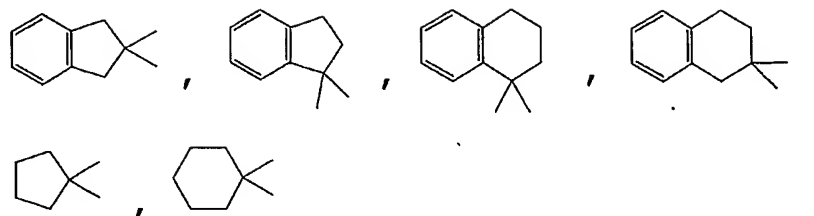
       Suitable example of "suitable substituent(s)" of "ar(lower)alkyl optionally substituted with one or more suitable 15 substituent(s)" for R<sup>3</sup> and R<sup>4</sup> may include lower alkoxy, lower alkyl, cyano, halogen, amino, nitro, carboxy and the like. The preferred "ar(lower)alkyl optionally substituted with one or more suitable substituent(s)" for R<sup>3</sup> and R<sup>4</sup> may include (4-methoxyphenyl)methyl, (4-ethoxyphenyl)methyl and the like.

20     Suitable "heterocyclic(lower)alkyl" for R<sup>3</sup> and R<sup>4</sup> may include, for example, indenylmethyl, pyridylmethyl, thienylmethyl, furylmethyl, imidazolylmethyl and the like.

       Suitable example of "suitable substituent(s)" of "heterocyclic(lower)alkyl optionally substituted with one or more 25 suitable substituent(s)" for R<sup>3</sup> and R<sup>4</sup> may be methyl, ethyl, alkoxy, cyano, halogen and the like, and the preferred "heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s)" for R<sup>3</sup> and R<sup>4</sup> may include N-methyl-2-indenylmethyl and the like.

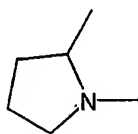
30     Suitable example of "cyclo(lower)alkyl(lower)alkyl" for R<sup>3</sup> and R<sup>4</sup> may be cyclohexylmethyl, cyclopentylmethyl and the like.

       Suitable example of "condensed ring" for R<sup>3</sup> and R<sup>4</sup> may be, for example,



and the like.

Suitable example of the "ring" of the "one of  $R^3$  and  $R^4$  is  
 5 linked to the adjacent nitrogen atom to form a ring" may be, for  
 example,



and the like.

Suitable "lower alkyl" for  $R^{11}$  may be methyl, ethyl and the like,  
 suitable "aryl" for  $R^{11}$  may be  $C_6$ - $C_{12}$  aryl such as phenyl and the like,  
 10 and suitable "ar(lower)alkyl" for  $R^{11}$  may be  $(C_6-C_{12})$ aryl( $C_1-C_6$ )alkyl  
 such as benzyl and the like.

Suitable "lower alkyl" for  $R^{12}$  may be methyl, ethyl, propyl  
 (e.g., isopropyl and the like), butyl (e.g., isobutyl, t-butyl and the  
 like), hexyl (e.g., n-hexyl) and the like, suitable "lower alkenyl"  
 15 for  $R^{12}$  may be vinyl and the like, and suitable "aryl" for  $R^{12}$  may be  
 $C_6$ - $C_{12}$  aryl such as phenyl and the like.

Suitable "lower alkyl" for  $R^{13}$  and  $R^{14}$  may be lower alkyl (e.g.,  
 methyl, ethyl and the like) and suitable "lower cycloalkyl" for  $R^{13}$  and  
 $R^{14}$  may be cyclohexyl and the like.

20 Suitable "ring" of the "ring wherein one or more methylene(s)  
 of the ring is(are) optionally replaced by heteroatom(s) selected from  
 an oxygen atom, a nitrogen atom and a sulfur atom" for  $R^{13}$  and  $R^{14}$  may  
 be piperidino, morpholino and the like.

Suitable "lower alkyl" for  $R^{15}$  may be lower alkyl. The  
 25 preferred one for  $R^{15}$  may be pentyl.

Suitable "lower alkyl" for  $R^{16}$  may be lower alkyl. The  
 preferred one for  $R^{16}$  may be methyl.

Suitable carboxy protective group may include:

- lower alkyl (e.g. methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-butyl, pentyl, hexyl and the like), preferably methyl, ethyl and t-butyl;
- mono(or di or tri)halo(lower)alkyl (e.g. 2-iodoethyl, 2,2,2-trichloroethyl and the like), preferably 2,2,2-trichloroethyl;
- lower alkanoyloxy(lower)alkyl (e.g. acetoxymethyl, propionyloxymethyl, butyryloxymethyl, valeryloxymethyl, pivaloyloxymethyl, hexanoyloxymethyl, 1(or 2)-acetoxyethyl, 1(or 2 or 3)-acetoxypentyl, 1(or 2 or 3 or 4)-acetoxybutyl, 1(or 2)-propionyloxyethyl, 1(or 2 or 3)-propionyloxypropyl, 1(or 2)-butyryloxyethyl, 1(or 2)-isobutyryloxyethyl, 1(or 2)-pivaloyloxyethyl, 1(or 2)-hexanoyloxyethyl, isobutyryloxymethyl, 2-ethylbutyryloxymethyl, 3,3-dimethylbutyryloxymethyl, 1(or 2)-pentanoyloxyethyl, and the like);
- lower alkanesulfonyl(lower)alkyl (e.g. 2-mesyloethyl and the like);
- lower alkoxycarbonyloxy(lower)alkyl (e.g. methoxycarbonyloxymethyl, ethoxycarbonyloxymethyl, 2-methoxycarbonyloxyethyl, 1-ethoxycarbonyloxyethyl, 1-isopropoxycarbonyloxyethyl, and the like);
- [5-(lower)alkyl-2-oxo-1,3-dioxol-4-yl](lower)alkyl (e.g. (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, (5-ethyl-2-oxo-1,3-dioxol-4-yl)methyl, (5-propyl-2-oxo-1,3-dioxol-4-yl)methyl, and the like);
- aryl optionally substituted with one or more suitable substituent(s) (e.g. phenyl, o(or m or p)-chlorophenyl, tolyl, o(or m or p)-t-butylphenyl, xylyl, mesityl, cumenyl, and the like);
- ar(lower)alkyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. benzyl, p-methoxybenzyl, o(or p)-nitrobenzyl, phenethyl, trityl, benzhydryl, bis(methoxyphenyl)methyl, m,p-dimethoxybenzyl, 4-hydroxy-3,5-di-t-butylbenzyl, and the like), preferably benzyl, p-methoxybenzyl and o(or p)-nitrobenzyl;
- arylcarbonyl(lower)alkyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. phenacyl and the like);
- cyclo(lower)alkyl (e.g. cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like);
- lower alkenyl (e.g. vinyl, allyl and the like), preferably allyl;
- lower alkynyl (e.g. ethynyl, propynyl, and the like);

- trisubstituted silyl such as tri(lower)alkylsilyl (e.g. trimethylsilyl, triethylsilyl, tributylsilyl, tert-butyldimethylsilyl, tri-tert-butylsilyl, and the like), lower alkyldiarylsilyl (e.g. methyldiphenylsilyl, ethyldiphenylsilyl, propyldiphenylsilyl, tert-butylsilyl, and the like), and the like, preferably trimethylsilyl, triethylsilyl, tert-butyldimethylsilyl and tert-butylsilyl;
- tri(lower)alkylsilyl(lower)alkyl (e.g. 2-(trimethylsilyl)ethyl and the like);
- 10 1-(lower)alkyl-2,6,7-trioxabicyclo[2.2.2]oct-4-yl (e.g. 1-methyl-2,6,7-trioxabicyclo[2.2.2]oct-4-yl, 1-ethyl-2,6,7-trioxabicyclo[2.2.2]oct-4-yl, and the like); and the like.
- Suitable hydroxy protective group may include:
- lower alkyl such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, 15 t-butyl, pentyl, hexyl, and the like, preferably methyl;
- lower alkoxy(lower)alkyl (e.g. methoxymethyl and the like);
- lower alkoxy(lower)alkoxy(lower)alkyl (e.g. 2-methoxyethoxymethyl and the like);
- ar(lower)alkyl in which the aryl portion is optionally substituted 20 with one or more suitable substituent(s) (e.g. benzyl (Bn), p-methoxybenzyl, m,p-dimethoxybenzyl, and the like), preferably benzyl;
- ar(lower)alkoxy(lower)alkyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. benzyloxymethyl, p-methoxybenzyloxymethyl, and the like);
- 25 (lower)alkylthio(lower)alkyl (e.g. methylthiomethyl, ethylthiomethyl, propylthiomethyl, isopropylthiomethyl, butylthiomethyl, isobutylthiomethyl, hexylthiomethyl, and the like), and the like, preferably methylthiomethyl;
- heterocyclic group (e.g. tetrahydropyranyl and the like);
- 30 trisubstituted silyl such as tri(lower)alkylsilyl (e.g. trimethylsilyl, triethylsilyl, tributylsilyl, tert-butyldimethylsilyl, tri-tert-butylsilyl, and the like), lower alkyldiarylsilyl (e.g. methyldiphenylsilyl, ethyldiphenylsilyl, propyldiphenylsilyl, tert-butylsilyl (TBDPS), and the like), and the like, preferably
- 35 tert-butyldimethylsilyl (TBDMS) and tert-butylsilyl;
- acyl as described below [e.g. aliphatic acyl such as lower alkanoyl

(e.g. acetyl, propanoyl, pivaloyl, and the like); aromatic acyl (e.g. benzoyl (Bz), toluoyl, naphthoyl, fluorenylcarbonyl and the like); lower alkoxycarbonyl (e.g. methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, isobutoxycarbonyl, 5 t-butoxycarbonyl, pentyloxycarbonyl, hexyloxycarbonyl, and the like), and the like;

ar(lower)alkoxycarbonyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. benzyloxycarbonyl, bromobenzyloxycarbonyl and the like);

10 lower alkylsulfonyl (e.g. methylsulfonyl, ethylsulfonyl, and the like);

lower alkoxysulfonyl (e.g. methoxysulfonyl, ethoxysulfonyl, and the like);

ar(lower)alkanoyl (e.g. phenylacetyl, phenylpropanoyl, phenylbutanoyl, 15 phenylisobutanoyl, phenylpentanoyl, phenylhexanoyl, naphthylacetyl, naphthylpropanoyl, naphthylbutanoyl, naphthylisobutanoyl, naphthylpentanoyl, naphthylhexanoyl, and the like);

ar(lower)alkenoyl such as ar(C<sub>3</sub>-C<sub>6</sub>)alkenoyl (e.g. phenylpropenoyl, phenylbutenoyl, phenylmethacryloyl, phenylpentenoyl, phenylhexenoyl, 20 naphthylpropenoyl, naphthylbutenoyl, naphthylmethacryloyl, naphthylpentenoyl, naphthylhexenoyl, and the like); and the like];

lower alkenyl (e.g. vinyl, allyl, and the like), preferably allyl; tetrahydropyranyl; and the like.

Suitable "amino protective group" may include:

25 acyl as exemplified for the hydroxy protective group;

ar(lower)alkyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g. benzyl, p-methoxybenzyl, o(or p)-nitrobenzyl, phenethyl, trityl, benzhydryl, bis(methoxyphenyl)methyl, m,p-dimethoxybenzyl, 4-hydroxy-3,5-di-t-

30 butylbenzyl, and the like);

[5-(lower)alkyl-2-oxo-1,3-dioxol-4-yl](lower)alkyl (e.g. (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, (5-ethyl-2-oxo-1,3-dioxol-4-yl)methyl, (5-propyl-2-oxo-1,3-dioxol-4-yl)methyl, and the like), and the like; and the like.

35 Suitable "acyl" for the present invention may be illustrated as follows:

- aliphatic acyl such as alkanoyl (e.g., formyl, acetyl, propanoyl, butanoyl, 2-methylpropanoyl, pentanoyl, pivaloyl, 2,2-dimethylpropanoyl, hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, undecanoyl, dodecanoyl, tridecanoyl, tetradecanoyl, pentadecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, nonadecanoyl, icosanoyl, and the like);
- alkoxycarbonyl (e.g., methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl, heptyloxycarbonyl, and the like);
- 10 alkylsulfonyl (e.g., methylsulfonyl, ethylsulfonyl, and the like);  
alkoxysulfonyl (e.g., methoxysulfonyl, ethoxysulfonyl, and the like);  
and the like;
- aromatic acyl such as aroyl (e.g., benzoyl, toluoyl, naphthoyl, fluorenylcarbonyl, and the like);
- 15 ar(lower)alkanoyl such as phenyl(lower)alkanoyl (e.g., phenylacetyl, phenylpropanoyl, phenylbutanoyl, phenylisobutanoyl, phenylpentanoyl, phenylhexanoyl, and the like), naphthyl(lower)alkanoyl (e.g., naphthylacetyl, naphthylpropanoyl, naphthylbutanoyl, and the like), and the like;
- 20 ar(lower)alkenoyl such as ar(C<sub>3</sub>-C<sub>6</sub>)alkenoyl (e.g., phenylpropenoyl, phenylbutenoyl, phenylmethacryloyl, phenylpentenoyl, phenylhexenoyl, and the like),  
naphthyl(C<sub>3</sub>-C<sub>6</sub>)alkenoyl (e.g., naphthylpropenoyl, naphthylbutenoyl, naphthylmethacryloyl, naphthylpentenoyl, naphthylhexenoyl, and the like), and the like;
- 25 ar(lower)alkoxycarbonyl such as phenyl(lower)alkoxycarbonyl (e.g., benzyloxycarbonyl, and the like), fluorenyl(lower)alkoxycarbonyl (e.g., fluorenylmethyloxycarbonyl, and the like), and the like;  
aryloxycarbonyl (e.g., phenoxycarbonyl, naphthyloxycarbonyl, and the like);
- 30 aryloxy(lower)alkanoyl (e.g., phenoxyacetyl, phenoxypropionyl, and the like);  
arylcarbamoyl (e.g., phenylcarbamoyl and the like);  
arylthiocarbamoyl (e.g., phenylthiocarbamoyl and the like);
- 35 arylglyoxyloyl (e.g., phenylglyoxyloyl, naphthylglyoxyloyl, and the like);

arylsulfonyl in which the aryl portion is optionally substituted with one or more suitable substituent(s) (e.g., phenylsulfonyl, p-tolylsulfonyl, and the like);

heterocyclic acyl (e.g. heterocycliccarbonyl and the like);

5 heterocyclic(lower)alkanoyl (e.g., heterocyclicacetyl, heterocyclicpropanoyl, heterocyclicbutanoyl, heterocyclicpentanoyl, heterocyclichexanoyl, and the like); heterocyclic(lower)alkenoyl (e.g., heterocyclicpropenoyl, heterocyclicbutenoyl, heterocyclicpentenoyl, heterocyclichexenoyl, and the like); heterocyclicglyoxyloyl; and the  
10 like.

Suitable "heterocyclic" moiety in the terms "heterocycliccarbonyl", "heterocyclic(lower)alkanoyl", heterocyclic(lower)alkenoyl" and "heterocyclicglyoxyloyl" is the same as the above-mentioned "heterocyclic" for the  
15 "heterocyclic(lower)alkyl" for R<sup>2</sup>.

Any "resin" known in the field of peptide synthesis may be used for the synthesis of the compound [I] of the present invention. Suitable example of the "resin" for the synthesis of the compound [I] includes 2-chlorotrityl resin and the like.

20 When the compound [I] has stereoisomers, such isomers are also encompassed in the present invention.

The compound [I] may form a salt, which is also encompassed in the present invention. For example, when a basic group such as an amino group is present in a molecule, the salt is exemplified by an  
25 acid addition salt (e.g. salt with an inorganic acid such as hydrochloric acid, hydrobromic acid, sulfuric acid, and the like, salt with an organic acid such as methanesulfonic acid, fumaric acid, maleic acid, mandelic acid, citric acid, salicylic acid, and the like) is exemplified, and when an acidic group such as carboxyl group is  
30 present, a basic salt (e.g. salt with a metal such as sodium, potassium, calcium, magnesium, aluminium, and the like, a salt with amino acid such as lysine, and the like), and the like.

In addition, solvates of the compound [I] such as hydrate, ethanolate, and the like, are also encompassed in the present  
35 invention.

Hereinafter the reactions in each Preparations and Examples for

preparing the cyclic tetrapeptide compound [I] of the present invention are explained in more detail. The invention should not be restricted by the following Preparations and Examples in any way.

#### Preparation A

##### 5 Preparation A-1

The compound (a-2) can be prepared by protecting the carboxyl group of the compound (a-1).

Suitable protective agent for the reaction may be, for example, benzylhalide (e.g. benzylbromide and the like), methyl iodide, ethyl  
10 iodide, substituted benzyl halide, and the like.

The reaction may be carried out in the presence of a base (e.g. cesium carbonate, potassium carbonate, sodium carbonate, sodium bicarbonate, triethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), pyridine, and the like).

15 The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. N,N-dimethylformamide, N-methylpyrrolidone, tetrahydrofuran, dimethylsulfoxide, and the like).

The reaction temperature is not critical and the reaction is usually carried out from under cooling to heating.

20 This Preparation is exemplified by Preparation 13 and the like.

##### Preparation A-2

The compound (a-3) can be prepared by 1) deprotecting the amino group of the compound (a-2) and 2) reacting the compound (a-2) with the compound (d-1).

25 1) Deprotection of the amino group of the compound (a-2)

Suitable deprotective agent for the reaction may be, for example, hydrogen chloride in suitable solvents (such as ethyl acetate, 1,4-dioxane, methanol, ethanol, and the like), trifluoroacetic acid, N,N-diethylamine, and the like. The deprotection may also be  
30 conducted with a hydrogenolysis catalyst (e.g. palladium on carbon (Pd-C), palladium hydroxide on carbon, and the like) under hydrogen atmosphere. Specifically, when the carboxyl protective group of the compound (a-2) is t-butyl (e.g. Compound (47)) and the like, the reaction is carried out in the presence of the above-mentioned  
35 hydrogenolysis catalyst under hydrogen atmosphere.

The reaction may be carried out in a conventional solvent which

does not adversely influence the reaction (e.g. ethyl acetate, dioxane, dichloromethane, acetonitrile, methanol, ethanol, tetrahydrofuran, acetic acid, and the like). Specifically, when trifluoroacetic acid is used as a deprotective agent, the reaction is generally carried out  
5 in dichloromethane or without solvent (neat).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating under the pressure of 1-5 atm.

Alternatively, the compound (a-2) in which the amino group is  
10 not protected, may be obtained by directly protecting the carboxyl group of D-proline, in substantially the same manner as Preparation A-1.

2) Reaction of the compound (a-2) with the compound (d-1)

The reaction may be carried out in the presence of carbodiimide  
15 [e.g. 1-ethyl-3-(3'-N,N-dimethylaminopropyl)-carbodiimide (EDC) or hydrochloride thereof, dicyclohexylcarbodiimide (DCC), and the like], benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (PyBOP®), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium hexafluoro phosphate (BOP), bromo-tris-pyrrolidinophosphonium  
20 hexafluorophosphate (PyBroP®), 1,1'-carbonyldiimidazol (CDI), diphenylphosphoryl azide (DPPA), 1-hydroxybenzotriazole (HOBT), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium-hexafluorophosphate (HATU), 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), and the  
25 like, and a base [e.g. Hünig base (e.g. N,N-diisopropylethylamine, triethylamine, and the like), and the like].

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, N,N-dimethylformamide, and the like).  
30

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 14 and the like.

Preparation A-3

35 The compound (a-4) can be prepared by 1) deprotecting the amino group of the compound (a-3) and 2) reacting the compound (a-3) with

the compound (d-2).

1) Deprotection of the amino group of the compound (a-3)

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2. Specifically, when the amino protective group is fluorenylmethyloxycarbonyl (Fmoc), a base such as N,N-diethylamine, piperidine, morpholine, dicyclohexylamine, 4-dimethylaminopyridine, N,N-diisopropylethyl amine and the like is used as a deprotective agent, and the reaction is generally carried out in a solvent such as N,N-dimethylformamide, acetonitrile, dichloromethane, and the like, or without solvent (neat).

2) Reaction of the compound (a-3) with the compound (d-2)

The reaction may be carried out in substantially the same manner as described above for the reaction of the compound (a-2) with the compound (d-1) in the Preparation A-2.

This Preparation is exemplified by Preparation 15 and the like.

Preparation A-4

The compound (a-5) can be prepared by 1) deprotecting the amino group of the compound (a-4) and 2) reacting the compound (a-4) with the compound (d-3).

1) Deprotection of the amino group of the compound (a-4)

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

2) Reaction of the compound (a-4) with the compound (d-3)

This reaction may be carried out in substantially the same manner as described above for the reaction of the compound (a-2) with the compound (d-1) in the Preparation A-2.

This Preparation is exemplified by Preparation 16 and the like.

Preparation A-5

The compound (a-6) can be prepared by deprotecting the carboxyl group of the compound (a-5).

The reaction may be carried out using a catalyst (e.g. Pearlman catalyst (Pd(OH)<sub>2</sub>-C), palladium on carbon (Pd-C), and the like) under hydrogen atmosphere. The reaction may also be carried out using an alkali (e.g. sodium hydroxide, potassium hydroxide, lithium hydroxide,

and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. methanol, ethanol, ethyl acetate, 1,4-dioxane, tetrahydrofuran, and the like).

5 The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This reaction is exemplified by Preparation 17 and the like.  
Preparation A-6

10 The compound [II] may be prepared by deprotecting the amino group of the compound (a-6).

The reaction may be carried out in substantially the same manner as described for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

This Preparation is exemplified by Preparation 18 and the like.  
15 Preparation A-5+6

Alternatively, when the carboxy protective group is t-butyl, the deprotection of carboxyl group and amino group of the compound (a-5) may be conducted simultaneously to give the Compound [II].

20 In this case, suitable deprotective agent for this reaction may be, for example, trifluoroacetic acid and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, and the like).

The temperature of the reaction is not critical and the  
25 reaction is usually carried out from under cooling to heating.

This reaction is exemplified by Preparation 53, 57 and the like.

The compound [II] as obtained above is used in the Preparation C.

Preparation B

30 Preparation B-1

The compound (b-2) may be prepared by reacting the compound (b-1) with the compound (d-4).

The reaction may be carried out in the presence of a base (e.g. diisopropylethylamine) in suitable solvent (e.g. dichloromethane,  
35 ethyl acetate, 1,4-dioxane, methanol, ethanol, and the like).

The reaction may be carried out in a conventional solvent which

does not adversely influence the reaction (e.g. dichloromethane and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

5        This Preparation is exemplified by Preparation 65 and the like.  
Preparation B-2

The compound (b-3) may be prepared by 1) deprotecting the amino group of the compound (b-2), and 2) reacting the compound (b-2) with the compound (d-1).

10    1) Deprotection of the amino group of the compound (b-2)

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

2) Reaction of the compound (b-2) with the compound (d-1)

15        The reaction may be carried out in the presence of PyBOP®, HATU, and the like, and a base (e.g. Hünig base (e.g. N,N-diisopropylethylamine and the like) and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. N,N-dimethylformamide and the like).

20        The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 66 and the like.

Preparation B-3

25        The compound (b-4) may be prepared by 1) deprotecting the amino group of the compound (b-3), and 2) reacting the compound (b-3) with the compound (d-2).

1) Deprotection of the amino group of the compound (b-3)

30        The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

2) Reaction of the compound (b-3) with the compound (d-2)

The reaction may be carried out in substantially the same manner as in Preparation B-2.

35        This Preparation is exemplified by Preparation 67 and the like.

Preparation B-4

The compound (b-5) may be prepared by 1) deprotecting the amino group of the compound (b-4), and 2) reacting the compound (b-4) with the compound (d-3).

- 5 1) Deprotection of the amino group of the compound (b-4)

The reaction may be carried out in substantially the same manner as described above for the deprotection of the amino group of the compound (a-2) in the Preparation A-2.

- 2) Reaction of the compound (b-4) with the compound (d-3)

- 10 The reaction may be carried out in the presence of PyBOP®, HATU, and the like, and a base (e.g. Hünig base (e.g. N,N-diisopropylethylamine and the like) and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, N,N-dimethylformamide, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 68 and the like.

Preparation B-5

- 20 The compound [II] may be prepared by deprotecting the amino group and the carboxyl group attached to the resin unit of the compound (b-5).

The reaction may be carried out in the presence of an acid (e.g. trifluoroacetic acid and the like).

- 25 The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

- 30 This Preparation is exemplified by Preparation 69 and the like.

The compound [II] is used in the Preparation C.

Preparation CPreparation C-1

- 35 The compound [III] may be prepared by cyclizing the compound [II].

The reaction may be carried out in the presence of a reagent

(e.g. HATU, BOP, PyBOP®, TBTU, HOBT, and the like), and a base (e.g. dimethylaminopyridine, triethylamine, N,N-diisopropylethylamine, and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. N,N-dimethylformamide, methylene chloride, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 76 and the like.

#### 10 Preparation C-2

The compound [IV] may be prepared by deprotecting the hydroxyl group of the compound [III].

The reaction may be carried out in the presence of a base (e.g. sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium methoxide, and the like).

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. methanol, ethanol, 1,4-dioxane, tetrahydrofuran, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 77 and the like.

#### Preparation C-3

The compound [V] may be prepared by oxidation of the compound [IV].

Suitable oxidizing agent in the reaction may be, for example, Dess-Martin periodinane (i.e. 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1H)-one), and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, dimethylsulfoxide, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

This Preparation is exemplified by Preparation 78 and the like.

The compound [V] is used in the Preparation of the compound [I] of the present invention.

#### Preparation of the compound [I] of the present invention

Preparation of the compound [I-1]

The compound [I-1] may be prepared by reacting the compound [V] with the compound (d-5).

Suitable compound (d-5) for the reaction may be, for example,  
5 dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxobutylphosphonate,  
dimethyl (3S)-tert-butyldimethylsilyloxy-2-oxobutylphosphonate,  
dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxoheptylphosphonate,  
dimethyl 3-fluoro-2-oxopropylphosphonate, and the like.

The reaction may be carried out in the presence of a base (e.g.  
10 barium hydroxide octahydrate, barium hydroxide monohydrate, sodium  
hydroxide, potassium tert-butoxide, cesium carbonate, and the like).

The reaction may be carried out in a conventional solvent which  
does not adversely influence the reaction (e.g. tetrahydrofuran,  
tetrahydrofuran-water mixture, N,N-dimethylformamide,  
15 dimethylsulfoxide, acetonitrile, ethanol, 2-propanol, and the like).

The temperature of the reaction is not critical and the  
reactions are usually carried out from under cooling to heating.

The reaction may also be carried out in the presence of an  
organic base (e.g. Hünig base, DBU; and the like) and a lithium salt  
20 (e.g. lithium chloride, lithium bromide, lithium iodide, and the like),  
in a suitable solvent (e.g. acetonitrile, dimethylformamide, and the  
like) [Horner-Wadsworth-Emmons reaction].

The temperature of the reaction is not critical and the  
reactions are usually carried out from under cooling to heating.

25 The Preparation of the compound [I-1] is exemplified by Example  
1 and the like.

Preparation of the compound [I-2]

The compound [I-2] may be prepared by hydrogenation of  
alkenylene of the compound [I-1'].

30 Suitable catalyst for the hydrogenation may be, for example,  
palladium-BaSO<sub>4</sub> (Pd-BaSO<sub>4</sub>), palladium on carbon (Pd-C), Pd(OH)<sub>2</sub> on  
carbon, and the like.

The reaction may be carried out in a conventional solvent which  
does not adversely influence the reaction (e.g. methanol, ethyl  
35 acetate, ethanol, 1,4-dioxane, and the like).

The temperature of the reaction is not critical and the

reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-2] is exemplified by Example 3 and the like.

Preparation of the compound [I-3]

5       The compound [I-3] may be prepared by deprotecting the hydroxyl group of the compound [I-1] or [I-2].

      Suitable agent for the reaction may be, for example, tetrabutylammonium fluoride, pyridinium poly(hydrogen fluoride), hydrogen fluoride, cesium fluoride, potassium fluoride, and the like.

10       The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. tetrahydrofuran, N,N-dimethylformamide, pyridine, and the like). Optionally, the reaction may be carried out in the presence of a catalyst (e.g. Pearlman catalyst ( $\text{Pd}(\text{OH})_2\text{-C}$ ), palladium on carbon ( $\text{Pd-C}$ ), and the like) under  
15       hydrogen atmosphere.

      The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

      The Preparation of the compound [I-3] is exemplified by Example 6 and the like.

20       To determine absolute configuration of the hydroxyl group of the compound [I-3] and to estimate optical purity of the isomer of the compound [I-3], the compound [I-3] is reacted with a reagent such as (R)-(-)- $\alpha$ -methoxy- $\alpha$ -trifluoromethyl- $\alpha$ -phenylacetyl chloride, (S)-(+)- $\alpha$ -methoxy- $\alpha$ -trifluoromethyl- $\alpha$ -phenylacetyl chloride, and the like.

25       The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. pyridine, methylene chloride, and the like).

      The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

30       This reaction is exemplified by Example 53.

Preparation of the compound [I-4]

      The compound [I-4] may be prepared by reacting the compound [I-3'] with sodium periodate.

      The reaction may be carried out in a conventional solvent which  
35       does not adversely influence the reaction (e.g. water, methanol, and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-4] is exemplified by Example 139 and the like.

5 Preparation of the compound [I-5]

The compound [I-5] may be prepared by reacting the compound [I-4] with the compound (d-6).

Suitable agent for the reaction may be, for example, carbodiimide [e.g. 1-ethyl-3-(3'-N,N-dimethylaminopropyl)-carbodiimide (EDC) or hydrochloride thereof, dicyclohexylcarbodiimide (DCC), and the like], benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (PyBOP®), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium hexafluoro phosphate (BOP), bromo-tris-pyrrolidinophosphonium hexafluorophosphate (PyBroP®), 1,1'-carbonyldiimidazol (CDI), diphenylphosphoryl azide (DPPA), 1-hydroxybenzotriazole (HOBT), benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium-hexafluorophosphate (HATU), 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, N,N-dimethylformamide and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-5] is exemplified by Example 141 and the like.

Preparation of the compound [I-6]

The compound [I-6] may be prepared by reacting the compound [I-5] with Grignard's agent [e.g. alkylmagnesium halide ( $R^{11}MgQ$ )].

Suitable alkylmagnesium halide for the reaction may be, for example, methyl magnesium bromide, ethyl magnesium bromide, phenyl magnesium bromide, benzyl magnesium bromide and the like.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. tetrahydrofuran, diethylether and the like).

The temperature of the reaction is, for example, -78°C to 0°C.

The Preparation of the compound [I-6] is exemplified by Example 143 and the like.

Preparation of the compound [I-7]

5       The compound [I-7] may be prepared by reducing the compound [I-1] with a reductant.

Suitable reductant for the reaction may be, for example, sodium borohydride, lithium aluminum hydride, diisobutylaluminum hydride, sodium cyanoborohydride, sodium triacetoxyborohydride and the like.

10       The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. methanol, ethanol, tetrahydrofuran, dioxane, 2-propanol and the like).

The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

15       The Preparation of the compound [I-7] is exemplified by Example 147 and the like.

Preparation of the compound [I-8]

20       The compound [I-8] may be prepared by fluoridation of a hydroxyl group of the compound [I-3'] with diethylaminosulfurtrifluoride.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g. dichloromethane, acetonitrile, acetic acid, chloroform, tetrahydrofuran, 2-propanol and the like).

25       The temperature of the reaction is not critical and the reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-8] is exemplified by Example 148 and the like.

Preparation of the compound [I-9]

30       The compound [I-9] may be prepared by reacting the compound [I-5] with alkyllithium ( $R^{12}Li$ ).

Suitable alkyllithium for the reaction may be, for example, n-butyllithium, methyllithium ethyllithium, isopropyllithium, isobutyllithium, tert-butyllithium, n-hexyllithium, phenyllithium, 35    vinylolithium and the like.

The reaction may be carried out in a conventional solvent which

does not adversely influence the reaction (e.g. tetrahydrofuran, diethyl ether, cyclohexane and the like).

The temperature of the reaction is, for example, -78°C to 0°C.

The Preparation of the compound [I-9] is exemplified by Example  
5 149 and the like.

Preparation of the compound [I-10]

The compound [I-10] may be prepared by reacting the compound  
[I-1''] with a secondary amine ( $R^{13}R^{14}NH$ ).

Suitable secondary amine for this reaction may be, for example,  
10 piperidine, morpholine, dicyclohexylamine, diethylamine and the like.

The reaction may be carried out in a conventional solvent which  
does not adversely influence the reaction (e.g. N,N-dimethylformamide,  
and the like).

The temperature of the reaction is not critical and the  
15 reaction is usually carried out from under cooling to heating.

Preparation of the compound [I-11]

The compound [I-11] may be prepared by reacting the compound  
[I-10] with methanesulfonyl chloride.

The reaction may be carried out in a conventional solvent which  
20 does not adversely influence the reaction (e.g. pyridine,  
dichloromethane, and the like).

The temperature of the reaction is, for example, 0°C to room  
temperature.

Preparation of the compound [I-12]

25 The compound [I-12] may be prepared by reacting the compound  
[I-10] with acetic anhydride in the presence of a catalytic amount of  
4-(dimethylamino)pyridine.

The reaction may be carried out in a conventional solvent which  
does not adversely influence the reaction (e.g. pyridine,  
30 dichloromethane and the like).

The temperature of the reaction is not critical and the  
reaction is usually carried out from under cooling to heating.

Preparation of the compound [I-13]

The compound [I-13] may be prepared by reacting the compound  
35 [I-3''] with sodium periodate under the catalytic amount of rubidium  
oxide.

The reaction may be carried out in a conventional solvent which does not adversely influence the reaction (e.g., a mixed solvent of carbon tetrachloride acetonitrile and water, and the like).

The temperature of the reaction is not critical and the  
5 reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-13] is exemplified by Example 163 and the like.

#### Preparation of the compound [I-14]

The compound [I-14] may be prepared by reacting the compound  
10 [I-13] with a primary amine ( $R^{15}-NH_2$ ).

The reaction may be carried out in the presence of PyBOP®, HATU, and the like, and a base (e.g. Hünig base (e.g. N,N-diisopropylethylamine and the like) and the like).

The reaction may be carried out in a conventional solvent which  
15 does not adversely influence the reaction (e.g. N,N-dimethylformamide and the like).

The temperature of the reaction is not critical and the  
reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-14] is exemplified by  
20 Example 164 and the like.

#### Preparation of the compound [I-15]

The compound [I-15] may be prepared by reacting the compound  
[I-3'''] with a primary amine ( $R^{16}-NH_2$ ).

The reaction may be carried out in a conventional solvent which  
25 does not adversely influence the reaction (e.g. methanol and the like).

The temperature of the reaction is not critical and the  
reaction is usually carried out from under cooling to heating.

The Preparation of the compound [I-15] is exemplified by  
Example 253 and the like.

#### 30 Test Method

In order to show the usefulness of the compound [I] of the invention, the pharmacological test result of the representative compounds of the present invention is shown in the following.

#### Test 1: Determination of histone deacetylase inhibitor activity

35 The partial purification of human histone deacetylase, the preparation of [ $^3H$ ] acetyl histones, and the assay for histone

deacetylase activity were performed basically according to the method as proposed by Yoshida et al. as follows.

Partial purification of human histone deacetylase

The human histone deacetylase was partially purified from human  
5 T cell leukemia Jurkat cells. Jurkat cells ( $5 \times 10^8$  cells) were  
suspended in 40 ml of the HDA buffer consisting of 15 mM potassium  
phosphate, pH 7.5, 5% glycerol and 0.2 mM EDTA. After homogenization,  
nuclei were collected by centrifugation ( $35,000 \times g$ , 10 min) and  
homogenized in 20 ml of the same buffer supplemented with 1 M  $(\text{NH}_4)_2\text{SO}_4$ .  
10 The viscous homogenate was sonicated and clarified by centrifugation  
( $35,000 \times g$ , 10 min), and the deacetylase was precipitated by raising  
the concentration of  $(\text{NH}_4)_2\text{SO}_4$  to 3.5 M. The precipitated protein was  
dissolved in 10 ml of the HDA buffer and dialyzed against 4 liters of  
the same buffer. The dialyzate was then loaded onto a DEAE-cellulose  
15 (Whatman DE52) column (25 x 85 mm) equilibrated with the same buffer  
and eluted with 300 ml of a linear gradient (0-0.6 M) of NaCl. A  
single peak of histone deacetylase activity appeared between 0.3 and  
0.4 M NaCl.

Preparation of [ $^3\text{H}$ ] acetyl histone

20 To obtain [ $^3\text{H}$ ] acetyl-labeled histone as the substrate for the  
histone deacetylase assay,  $1 \times 10^8$  cells of Jurkat in 20 ml of RPMI-  
1640 medium (supplemented with 10% FBS, penicillin (50 units/ml) and  
streptomycin (50  $\mu\text{g}/\text{ml}$ )) were incubated with 300 MBq [ $^3\text{H}$ ] sodium  
acetate in the presence of 5 mM sodium butyrate for 30 minutes in 5%  
25  $\text{CO}_2$ -95% air atmosphere at  $37^\circ\text{C}$  in a  $75 \text{ cm}^2$  flask, harvested into a  
centrifuge tube (50 ml), collected by centrifugation at 1000 rpm for  
10 minutes, and washed once with phosphate-buffered saline. The  
washed cells were suspended in 15 ml of ice-cold lysis buffer (10 mM  
Tris-HCl, 50 mM sodium bisulfite, 1% Triton X-100, 10 mM  $\text{MgCl}_2$ , 8.6%  
30 sucrose, pH 6.5). After Dounce homogenization (30 stroke), the nuclei  
were collected by centrifugation at 1000 rpm for 10 minutes, washed 3  
times with 15 ml of the lysis buffer, and once with 15 ml of ice-  
cooled washing buffer (10 mM Tris-HCl, 13 mM EDTA, pH 7.4)  
successively. The pellet was suspended in 6 ml of ice-cooled water  
35 using a mixer, and 68  $\mu\text{l}$  of  $\text{H}_2\text{SO}_4$  was added to the suspension to give a  
concentration of 0.4 N. After incubation at  $4^\circ\text{C}$  for 1 hour, the

suspension was centrifuged for 5 minutes at 15,000 rpm, and the supernatant was taken and mixed with 60 ml of acetone. After overnight incubation at -20°C, the coagulated material was collected by microcentrifugation, air-dried, and stored at -80°C.

5 Assay for histone deacetylase activity

For the standard assay, 10 µl of [<sup>3</sup>H] acetyl-labeled histones were added to 90 µl of the enzyme fraction, and the mixture was incubated at 25°C for 30 minutes. The reaction was stopped by addition of 10 µl of HCl. The released [<sup>3</sup>H] acetic acid was extracted with 1 ml of ethyl acetate, and 0.9 ml of the solvent layer was taken into 10 ml of toluene scintillation solution for determination of radioactivity.

Test 2: Determination of T-cell growth inhibitor activity

The T lymphocyte blastogenesis test was performed in microtiter plates with each well containing  $1.5 \times 10^5$  splenic cells of Lewis rats in 0.1 ml RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS), 50 mM 2-mercaptoethanol, penicillin (100 units/ml) and streptomycin (100 µg/ml), to which Concanavalin A (1 µg/ml) was added. The cells were incubated at 37°C in a humidified atmosphere of 5% CO<sub>2</sub> for 72 hours. After the culture period, suppressive activities of the test compounds in T lymphocyte blastogenesis were quantified by AlamarBlue (trademark) Assay. The test samples were dissolved in DMSO and further diluted with RPMI-1640 medium and added to the culture. The activities of the test compounds were expressed as IC<sub>50</sub>.

25 The results of those tests are shown in the Table 1.

Table 1: HDAC inhibitory activity and T-cell growth inhibitory activity of the compound of the present invention

Examples	<u>Test 1</u> : HDAC inhibitory activity IC <sub>50</sub> (nM)	<u>Test 2</u> : T-cell growth inhibitory activity IC <sub>50</sub> (nM)
Compound E6	<100	<50
Compound E8	<100	<50
Compound E13	<100	<50
Compound E17	<100	<50
Compound E23	<100	<50
Compound E26	<100	<50
Compound E33	<100	<50
Compound E35	<100	<50
Compound E38	<100	<50
Compound E41	<100	<50
Compound E48	<100	<50

Test 3: Effect of HDAC inhibitor on TNF $\alpha$  induced NF- $\kappa$ B activation

5        8.75 x 10<sup>6</sup> HEL cells (JCRB0062, JCRB) were transfected with 10  
 10         $\mu$ g of pNF $\kappa$ B-TA-Luc (Clontech, as shown in Fig.1) by electroporation at  
 1750 V and 10  $\mu$ F with Gene Pulser II (BIO-RAD). The cells were  
 resuspended in 2 ml of RPMI1640 (SIGMA) supplemented with 10% FBS  
 (MOREGATE) and aliquated 50  $\mu$ l each well in 96-well tissue culture  
 15        plates. After 5 hr culture at 37°C, 5% CO<sub>2</sub>, for cell function recovery,  
 the cells were cultured in the presence or absence of TNF $\alpha$  (10 ng/ml)  
 for 4 hr. TNF $\alpha$  stimulated cells were incubated with Compound E138 or  
 FK506 (commercial available immunosuppressive agent, also referred as  
 Tacrolimus) at appropriate concentrations for 1 hour prior to  
 stimulation.

For the NF- $\kappa$ B reporter gene assay, the transfected cells were  
 lysed and assayed for luciferase activity with the Bright-glo  
 Luciferase Assay System (Promega) according to the manufacturer's  
 instructions.

20        For the cell growth analysis, the transfected cells were  
 analyzed using Cell Counting Kit8 (Dojin) according to the  
 manufacturer's instructions.

Results of the study are shown in Fig.2. Treatment of the transfected cells with TNF $\alpha$  induces NF- $\kappa$ B-dependent luciferase expression. Compound E138 has an inhibitory effect on TNF $\alpha$  induced NF- $\kappa$ B activation in a dose-dependent manner without affecting cell growth. In contrast to the effect of Compound E138, FK506 has no direct effect on TNF $\alpha$  induced NF- $\kappa$ B activation at doses up to 3 nM (FK506 almost completely inhibits IL-2 mRNA expression in activated Jurkat cells at 1 nM). Therefore, HDAC inhibitor (Compound E138) has an inhibitory effect on NF- $\kappa$ B activation induced by TNF $\alpha$ , a calcium-signaling-independent NF- $\kappa$ B activation, whereas FK506 has no direct effect on it.

Test 4: Effect of HDAC inhibitor on MCP-1 production by activated THP-1 cells

For the measurement of MCP-1 level by ELISA, 1 x 10<sup>6</sup> THP-1 cells (JCRB0112, JCRB) were plated in 6-well tissue culture plates. The cells were cultured in RPMI1640 (SIGMA) supplemented with 10% FBS (MOREGATE) in the presence of PMA (SIGMA, 50 ng/mL) for 16 hours at 37°C, 5% CO<sub>2</sub>. After incubation, the medium was changed to RPMI1640 supplemented with 2% FBS and various concentrations of Compound E138 or FK506 were added. The cells were further cultured for 9 hr and the amount of MCP-1 protein secreted by activated THP-1 cells into the medium was determined by ANALYZA Immuno assay System human MCP-1 (Genzyme Techne) according to the manufacturer's instructions.

For the cell growth analysis, 5 x 10<sup>4</sup> THP-1 cells were plated in 96-well tissue culture plates. The cells were cultured in RPMI1640 supplemented with 10% FBS in the presence of PMA (50 ng/mL) for 16 hours at 37°C, 5% CO<sub>2</sub>. After incubation, the medium was changed to RPMI1640 supplemented with 2% FBS and various concentrations of Compound E138 or FK506 were added. The cells were further cultured for 9 hr and analyzed using Cell Counting Kit8 (Dojin) according to the manufacturer's instructions.

Results of the study are shown in Fig.3. Treatment of the cells with PMA induces MCP-1 expression. Compound E138 has an inhibitory effect on MCP-1 production by activated THP-1 cells in a dose-dependent manner without affecting cell growth. In contrast to the effect of Compound E138, FK506 has no direct effect on MCP-1

production by activated THP-1 cells at doses up to 1 nM (FK506 almost completely inhibits IL-2 mRNA expression in activated Jurkat cells at 1 nM).

These results demonstrate that HDAC inhibitors such as Compound  
5 El38 is a new class of the immunosuppressive agents that inhibit MCP-1-dependent chronic inflammation.

The pharmaceutical composition of the present invention comprising histone deacetylase inhibitor, such as the compound [I], is useful as a therapeutic or prophylactic agent for diseases caused by  
10 abnormal gene expression, such as inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), protozoal infection and the like. Further, it is useful as an antitumor agent or immunosuppressant, which prevents an organ transplant rejection and autoimmune diseases  
15 as exemplified below.

Rejection reactions by transplantation of organs or tissues such as the heart, kidney, liver, bone marrow, skin, cornea, lung, pancreas, small intestine, limb, muscle, nerve, intervertebral disc, trachea, myoblast, cartilage, and the like;  
20 graft-versus-host reactions following bone marrow transplantation; autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, type I diabetes, and the like; and infections caused by pathogenic microorganisms (e.g. Aspergillus fumigatus, Fusarium oxysporum, Trichophyton asteroides, and the like).  
25

Furthermore, pharmaceutical preparations of the histone deacetylase inhibitor, such as the compound [I], are useful for the therapy or prophylaxis of the following diseases.

Inflammatory or hyperproliferative skin diseases or cutaneous  
30 manifestations of immunologically-mediated diseases (e.g. psoriasis, atopic dermatitis, contact dermatitis, eczematoid dermatitis, seborrheic dermatitis, lichen planus, pemphigus, bullous pemphigoid, epidermolysis bullosa, urticaria, angioedema, vasculitides, erythema, dermal eosinophilia, lupus erythematosus, acne, and alopecia areata);  
35 autoimmune diseases of the eye (e.g. keratoconjunctivitis, vernal conjunctivitis, uveitis associated with Behcet's disease, keratitis,

- herpetic keratitis, conical keratitis, corneal epithelial dystrophy, keratoleukoma, ocular pemphigus, Mooren's ulcer, scleritis, Grave's ophthalmopathy, Vogt-Koyanagi-Harada syndrome, keratoconjunctivitis sicca (dry eye), phlyctenule, iridocyclitis, sarcoidosis, endocrine ophthalmopathy, and the like);
- reversible obstructive airways diseases [asthma (e.g. bronchial asthma, allergic asthma, intrinsic asthma, extrinsic asthma, and dust asthma), particularly chronic or inveterate asthma (e.g. late asthma and airway hyper-responsiveness) bronchitis, and the like];
- mucosal or vascular inflammations (e.g. gastric ulcer, ischemic or thrombotic vascular injury, ischemic bowel diseases, enteritis, necrotizing enterocolitis, intestinal damages associated with thermal burns, leukotriene B<sub>4</sub>-mediated diseases);
- intestinal inflammations/allergies (e.g. coeliac diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, Crohn's disease and ulcerative colitis);
- food-related allergic diseases with symptomatic manifestation remote from the gastrointestinal tract (e.g. migraine, rhinitis and eczema);
- renal diseases (e.g. interstitial nephritis, Goodpasture's syndrome, hemolytic uremic syndrome, and diabetic nephropathy);
- nervous diseases (e.g. multiple myositis, Guillain-Barre syndrome, Meniere's disease, multiple neuritis, solitary neuritis, cerebral infarction, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis (ALS), and radiculopathy);
- cerebral ischemic diseases (e.g., head injury, hemorrhage in brain (e.g., subarachnoid hemorrhage, intracerebral hemorrhage), cerebral thrombosis, cerebral embolism, cardiac arrest, stroke, transient ischemic attack (TIA), and hypertensive encephalopathy);
- endocrine diseases (e.g. hyperthyroidism, and Basedow's disease);
- hematic diseases (e.g. pure red cell aplasia, aplastic anemia, hypoplastic anemia, idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia, agranulocytosis, pernicious anemia, megaloblastic anemia, and anerythroplasia);
- bone diseases (e.g. osteoporosis);
- respiratory diseases (e.g. sarcoidosis, pulmonary fibrosis, and idiopathic interstitial pneumonia);

- skin diseases (e.g. dermatomyositis, leukoderma vulgaris, ichthyosis vulgaris, photosensitivity, and cutaneous T-cell lymphoma);  
circulatory diseases (e.g. arteriosclerosis, atherosclerosis, aortitis syndrome, polyarteritis nodosa, and myocardosis);
- 5 collagen diseases (e.g. scleroderma, Wegener's granuloma, and Sjögren's syndrome);  
adiposis;  
eosinophilic fasciitis;  
periodontal diseases (e.g. damage to gingiva, periodontium, alveolar
- 10 bone or substantia ossea dentis);  
nephrotic syndrome (e.g. glomerulonephritis);  
male pattern alopecia, alopecia senile;  
muscular dystrophy;  
pyoderma and Sezary syndrome;
- 15 chromosome abnormality-associated diseases (e.g. Down's syndrome);  
Addison's disease;  
active oxygen-mediated diseases [e.g. organ injury (e.g. ischemic circulation disorders of organs (e.g. heart, liver, kidney, digestive tract, and the like) associated with preservation, transplantation, or
- 20 ischemic diseases (e.g. thrombosis, cardiac infarction, and the like);  
intestinal diseases (e.g. endotoxin shock, pseudomembranous colitis, and drug- or radiation-induced colitis);  
renal diseases (e.g. ischemic acute renal insufficiency, chronic renal failure);
- 25 pulmonary diseases (e.g. toxicosis caused by pulmonary oxygen or drugs (e.g. paracort, bleomycin, and the like), lung cancer, and pulmonary emphysema);  
ocular diseases (e.g. cataracta, iron-storage disease (siderosis bulbi), retinitis, pigmentosa, senile plaques, vitreous scarring,
- 30 corneal alkali burn);  
dermatitis (e.g. erythema multiforme, linear immunoglobulin A bullous dermatitis, cement dermatitis);  
and other diseases (e.g. gingivitis, periodontitis, sepsis, pancreatitis, and diseases caused by environmental pollution (e.g. air
- 35 pollution), aging, carcinogen, metastasis of carcinoma, and hypobaropathy)];

diseases caused by histamine release or leukotriene C4 release;  
restenosis of coronary artery following angioplasty and prevention of  
postsurgical adhesions;

autoimmune diseases and inflammatory conditions (e.g., primary mucosal  
5 edema, autoimmune atrophic gastritis, premature menopause, male  
sterility, juvenile diabetes mellitus, pemphigus vulgaris, pemphigoid,  
sympathetic ophthalmitis, lens-induced uveitis, idiopathic leukopenia,  
active chronic hepatitis, idiopathic cirrhosis, discoid lupus  
erythematosus, autoimmune orchitis, arthritis (e.g. arthritis  
10 deformans), or polychondritis);  
Human Immunodeficiency Virus (HIV) infection, AIDS;  
allergic conjunctivitis;  
hypertrophic cicatrix and keloid due to trauma, burn, or surgery.

Therefore, the pharmaceutical composition of the present  
15 invention is useful for the therapy and prophylaxis of liver diseases  
[e.g. immunogenic diseases (e.g. chronic autoimmune liver diseases  
such as autoimmune hepatic diseases, primary biliary cirrhosis or  
sclerosing cholangitis), partial liver resection, acute liver necrosis  
(e.g. necrosis caused by toxins, viral hepatitis, shock, or anoxia),  
20 hepatitis B, non-A non-B hepatitis, hepatocirrhosis, and hepatic  
failure (e.g. fulminant hepatitis, late-onset hepatitis and "acute-on-  
chronic" liver failure (acute liver failure on chronic liver  
diseases))].

The pharmaceutical composition of the present invention can be  
25 used in the form of pharmaceutical preparation, for example, in a  
solid, semisolid or liquid form, which contains the histone  
deacetylase inhibitor, such as the compound [I], as an active  
ingredient in admixture with an organic or inorganic carrier or  
excipient suitable for external, enteral or parenteral administrations.  
30 The active ingredient may be compounded, for example, with the usual  
non-toxic, pharmaceutically acceptable carriers for tablets, pellets,  
capsules, suppositories, solutions, emulsions, suspensions, injections,  
ointments, liniments, eye drops, lotion, gel, cream, and any other  
form suitable for use.

35 The carriers which can be used are water, glucose, lactose, gum  
acacia, gelatin, mannitol, starch paste, magnesium trisilicate, talc,

corn starch, keratin, colloidal silica, potato starch, urea and other carriers suitable for use in manufacturing preparations, in a solid, semisolid, or liquid form, and in addition auxiliary, stabilizing, thickening, solubilizing and coloring agents and perfumes may be used.

5 For applying the composition to human, it is preferable to apply it by intravenous, intramuscular, topical or oral administration, or by a vascular stent impregnated with the compound [I]. While the dosage of therapeutically effective amount of the histone deacetylase inhibitor, such as the compound [I], varies from and also depends upon  
10 the age and condition of each individual patient to be treated, when an individual patient is to be treated, in the case of intravenous administration, a daily dose of 0.01-10 mg of the histone deacetylase inhibitor, such as the compound [I], per kg weight of human being, in the case of intramuscular administration, a daily dose of 0.1-10 mg of  
15 the histone deacetylase inhibitor, such as the compound of the formula [I], per kg weight of human being, and in the case of oral administration, a daily dose of 0.5-50 mg of the histone deacetylase inhibitor, such as the compound [I], per kg weight of human being, is generally given for treatment.

20 During the preparation of the above-mentioned pharmaceutical administration forms, the compound [I] or a salt thereof can also be combined together with other immunosuppressive substances, for example repamycin, mycophenolic acid, cyclosporin A, tacrolimus or brequinar sodium.

25 The following Preparations and Examples are given for the purpose of illustrating the present invention in more detail.

#### Preparation 1

To a stirred solution of 2(S)-(+)-amino-2-methylbutanoic acid monohydrate (15 g) in 1,4-dioxane (225 ml), a mixture of 1N sodium  
30 hydroxide aqueous solution (111 ml) and di-tert-butyl dicarbonate (24.2 g) was added at ambient temperature and the resulting mixture was stirred for 53 hours. Additional mixture of di-tert-butyl dicarbonate (24.2 g) and 1N sodium hydroxide aqueous solution (111 ml) was added at 8 hours, 24 hours and 48 hours after the start of the  
35 reaction. The mixture was diluted with diethyl ether (400 ml) and the organic layer was separated. The pH of the aqueous phase was adjusted

to 1 with concentrated hydrochloric acid. The aqueous phase was extracted with ethyl acetate (500 ml) twice and the organic layers were combined, washed with brine (500 ml), dried over anhydrous sodium sulfate and concentrated in vacuo. The residual solid was treated  
5 with hexane (100 ml) and the resulting suspension was stirred in an ice bath for one hour. The precipitate was filtered and washed with cold hexane to afford 2(S)-N-tert-butoxycarbonylamino-2-methylbutanoic acid (21.71 g, hereinafter Compound (1)) as a white amorphous solid.  
<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 6.82 (1H, brs), 1.61-1.82 (2H, m), 1.36  
10 (9H, s), 0.75 (3H, t, J=7.5 Hz);  
MASS (ES-): m/e 216.17.

#### Preparation 2

To a solution of (S)-2-amino-6-hydroxyhexanoic acid (2.0 g) and sodium bicarbonate (2.28 g) in dioxane-water mixture (20 ml : 20 ml)  
15 was added di-tert-butyl dicarbonate (5.93 g) at room temperature. The resulting mixture was stirred at room temperature for 6 hours. The reaction mixture was diluted with water and washed with ether. The aqueous phase was adjusted to pH 2 with conc. hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with water  
20 and brine, dried over anhydrous sodium sulfate and concentrated in vacuo to give 2(S)-N-tert-butoxycarbonylamino-6-hydroxyhexanoic acid as a solid.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.18-1.45 (4H, m), 1.37 (9H, s), 1.45-1.70 (2H, m), 3.35 (2H, m), 3.75-3.88 (1H, m), 4.31-4.45 (1H, br),  
25 7.06 (1H, d, J=7.5 Hz);  
MASS (ES-): m/e 246.15 (M-1).

#### Preparation 3

To a solution of 2(S)-N-tert butoxycarbonylamino-6-hydroxyhexanoic acid (3.36 g) in N,N-dimethylformamide (35 ml), cesium  
30 carbonate powder was added (2.21 g) at 0°C and stirred for 1.5 hours at room temperature. To the mixture, benzylbromide (1.66 ml) was added at 0°C and stirred for 1.5 hours. The reaction mixture was stirred for further 1.5 hours at room temperature. The reaction mixture was poured into water under ice-cooling and extracted with  
35 ethyl acetate. The organic layer was washed with water (3 times) and brine, dried over anhydrous sodium sulfate and concentrated in vacuo

to give 2(S)-N-tert-butoxycarbonylamino-6-hydroxyhexanoic acid benzyl ester as a pale yellow crude oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.44 (9H, s), 1.48-1.90 (7H, m), 3.55-3.65 (2H, m), 4.30-4.41 (1H, m), 5.02-5.10 (1H, m), 5.10-5.25 (2H, m), 7.36 (5H, brs);

MASS (ES<sup>-</sup>): m/e 338.23 (M+1).

#### Preparation 4

To a solution of 2(S)-N-tert-butoxycarbonylamino-6-hydroxyhexanoic acid benzyl ester (4.58 g) in pyridine (13 ml), benzoylchloride (2 g) was added at 0°C and stirred for 1.5 hours at room temperature. The reaction mixture was poured into cooled 1N hydrochloric acid (150 ml) and stirred for 10 minutes. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with water, saturated aqueous sodium bicarbonate solution, water and brine, dried over anhydrous sodium sulfate and concentrated in vacuo. The crude product was purified by column chromatography (eluting with ethyl acetate/hexane = 10/1 to 4/1 v/v) to give 2(S)-N-tert-butoxycarbonylamino-6-benzoyloxyhexanoic acid benzyl ester as a pale yellow oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.35-1.60 (2H, m), 1.43 (9H, s), 1.62-1.96 (4H, m), 4.26 (1H, t, J=6.0 Hz), 4.30-4.42 (1H, m), 5.00-5.08 (1H, m), 5.08-5.22 (2H, m), 7.34 (5H, s), 7.39-7.46 (2H, m), 7.52-7.60 (1H, m), 7.98-8.05 (2H, m);

MASS (ES<sup>+</sup>): m/e 442.34.

#### Preparation 5

To a solution of 2(S)-N-tert-butoxycarbonylamino-6-benzoyloxyhexanoic acid benzyl ester (5.43 g) in methanol (55 ml), palladium hydroxide on charcoal catalyst (50 mg) was added. The air atmosphere was replaced with hydrogen (4 atm) and shaken for 3 hours. The resulting mixture was filtered through a pad of Celite®, and washed with methanol. The filtrate was concentrated in vacuo to give 6-benzoyloxy-2(S)-N-tert-butoxycarbonylamino-6-hydroxyhexanoic acid (hereinafter Compound (5)) as a pale yellow oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.44 (9H, s), 1.47-2.05 (6H, m), 4.12-4.27 (1H, m), 4.44 (2H, t, J=6.0 Hz), 5.00-5.12 (1H, m), 7.38-7.50 (2H, m), 7.50-7.62 (1H, m), 8.00-8.07 (2H, m);

MASS (ES+): m/e 352.20 (M+1).

#### Preparation 6

To a cooled suspension of N-tert-butoxycarbonylamino-6-methoxy-6-oxo-L-norleucine dicyclohexylamine salt (21.1 g) in N,N-dimethylformamide (210 ml) was added benzyl bromide (7.9 g), and the mixture was stirred at ambient temperature for 3 days. The mixture was evaporated in vacuo. The residue was diluted with ethyl acetate and the remaining solid was filtered off. The filtrate was washed with 10% aqueous citric acid solution, saturated aqueous sodium bicarbonate solution and brine, dried over magnesium sulfate and evaporated in vacuo. The residue was purified by silica gel column chromatography (eluting with hexane/ethyl acetate = 4:1 to 2:1 v/v) to give N-tert-butoxycarbonyl-6-methoxy-6-oxo-L-norleucine benzyl ester (15.4 g) as a white solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.28 (3x3H, s), 1.59-1.75 (3H, m), 1.83 (1H, m), 2.31 (2H, m), 3.65 (3H, s), 4.35 (1H, m), 5.06 (1H, brd, J=8 Hz), 5.14 (1H, d, J=12 Hz), 5.20 (1H, d, J=12 Hz), 7.30-7.42 (5H, m);

MASS (ES+): m/e 366.

#### Preparation 7

To a stirred solution of N-tert-butoxycarbonyl-6-methoxy-6-oxo-L-norleucine benzyl ester (15.4 g) in acetonitrile (150 ml) were added 4-dimethylaminopyridine (1.03 g) and di-tert-butylidicarbonate (14.7 g), and the mixture was stirred at ambient temperature for 1 day. The mixture was evaporated in vacuo. The residue was purified by silica gel column chromatography (eluting with hexane/ethyl acetate = 10:1 v/v) to give N,N-di-tert-butoxycarbonyl-6-methoxy-6-oxo-L-norleucine as a colorless oil (20.0 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.45 (2x9H, s), 1.70 (2H, m), 1.96 (1H, m), 2.15 (1H, m), 2.36 (2H, m), 3.66 (3H, s), 4.90 (1H, dd, J=9, 4.5 Hz), 5.13 (1H, d, J=11 Hz), 5.17 (1H, d, J=11 Hz), 7.28-7.39 (5H, m);

MASS (ES+): m/e 488.

#### Preparation 8

To a cooled solution of N,N-di-tert-butoxycarbonyl-6-methoxy-6-oxo-L-norleucine (9.71 g) in diethyl ether (150 ml) was added dropwise 1M solution of diisobutylaluminium hydride in hexane (DIBAL) (23 ml) at -78°C. After 30 minutes DIBAL (24 ml) was added dropwise until the

starting compound was disappeared. The reaction mixture was quenched by addition of water. After warming to 0°C with stirring, the mixture was filtered through a pad of Celite®. The solvent was evaporated and the residual solvent was removed azeotropically with toluene to give  
5 N,N-di-tert-butoxycarbonyl-6-oxo-L-norleucine benzyl ester as a pale yellow oil (8.94 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.45 (2x9H, s), 1.70 (2H, m), 1.96 (1H, m), 2.14 (1H, m), 2.49 (2H, m), 4.90 (1H, m), 5.13 (1H, d, J=12 Hz), 5.17 (1H, d, J=12 Hz), 7.26-7.39 (5H, m), 9.76 (1H, t, J=1 Hz);

10 MASS (ES-): m/e 435.

#### Preparation 9

To a stirred solution of dimethyl (3R)-3-benzyloxy-2-oxobutylphosphonate (1.08 g), lithium chloride (174 mg), and N,N-diisopropylethylamine (442 mg) in acetonitrile (10 ml) was added a  
15 solution of N,N-di-tert-butoxycarbonyl-6-oxo-L-norleucine benzyl ester (1.49 g) in acetonitrile (30 ml) at ambient temperature. The mixture was stirred at ambient temperature for 5 days. After evaporation of the solvent, the residue was diluted with water, and extracted with ethyl acetate. The extract was washed with brine, dried over  
20 magnesium sulfate, and the solvent was evaporated in vacuo. The residue was purified by silica gel column chromatography (eluting with hexane/ethyl acetate = 10:1 v/v) to give benzyl (2S, 6E)-9-benzyloxy-2-di-tert-butoxycarbonylamino-8-oxodec-6-enoate as an oil (1.13 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.35 (3H, d, J=7 Hz), 1.38-1.62 (6H, m),  
25 1.44 (2x9H, s), 1.95 (1H, m), 2.16 (1H, m), 2.28 (2H, m), 4.05 (1H, q, J=7 Hz), 4.41 (1H, d, J=12 Hz), 4.56 (1H, d, J=12 Hz), 4.90 (1H, dd, J=10 and 5 Hz), 5.12 (1H, d, J=12 Hz), 5.16 (1H, d, J=12 Hz), 6.51 (1H, d, J=15 Hz), 7.02 (1H, dt, J=15, 7 Hz), 7.23-7.40 (5H, m);

MASS (ES+): m/e 618 (M+Na).

#### 30 Preparation 10

A solution of benzyl (2S, 6E)-9-benzyloxy-2-di-tert-butoxycarbonylamino-8-oxodec-6-enoate (2.74 g) in ethyl acetate (30 ml) was hydrogenated in the presence of 10% palladium-carbon (300 mg) for 2 hours. The reaction mixture was filtered through a pad of  
35 Celite® and concentrated in vacuo to give (2S)-9-benzyloxy-2-di-tert-butoxycarbonylamino-8-oxodecanoic acid as an oil (2.27 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.19-1.53 (6H, m), 1.33 (3H, d, J=7 Hz), 1.50 (2x9H, s), 1.89 (1H, m), 2.07 (1H, m), 2.44-2.65 (2H, m), 3.92 (1H, q, J=7 Hz), 4.48 (1H, d, J=12 Hz), 4.54 (1H, d, J=12 Hz), 4.89 (1H, dd, J=10, 5 Hz), 7.22-7.40 (5H, m);

5 MASS (ES-): m/e 506.

#### Preparation 11

To a solution of (2S)-9-benzyloxy-2-di-tert-butoxycarbonylamino-8-oxodecanoic acid (164 mg) in dioxane (2 ml) was added 4N-hydrogen chloride in dioxane (2 ml), and the mixture was stirred at ambient  
10 temperature for 3 hours. The solvent was evaporated in vacuo and the residual solvent was removed azeotropically with toluene to give (2S)-2-amino-9-benzyloxy-8-oxodecanoic acid hydrochloride as an amorphous (109 mg).

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.16-1.53 (6H, m), 1.23 (3H, d, J=7 Hz),  
15 1.76 (2H, m), 2.55 (2H, m), 3.86 (1H, t, J=5 Hz), 3.99 (1H, q, J=7 Hz), 4.46 (1H, d, J=12 Hz), 4.51 (1H, d, J=12 Hz), 7.26-7.41 (5H, m), 8.30 (2H, br);

MASS (ES+): m/e 308.

#### Preparation 12

To a stirred solution of (2S)-2-amino-9-benzyloxy-8-oxodecanoic acid hydrochloride (1.37 g) in dioxane (20 ml) were added 1N-sodium hydroxide (8.8 ml) and di-tert-butylidicarbonate (1.04 g) in dioxane, and the mixture was stirred at ambient temperature for 4 hours. The mixture was concentrated in vacuo. The residue was diluted with water  
25 and the mixture was washed with diethyl ether. The aqueous phase was acidified with 1N-hydrogen chloride, and extracted with ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate, and evaporated in vacuo to give (2S)-9-benzyloxy-2-tert-butoxycarbonylamino-8-oxodecanoic acid (hereinafter Compound (12)) as  
30 a colorless oil (1.48 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.21-1.46 (4H, m), 1.33 (3H, d, J=7 Hz), 1.52-1.74 (3H, m), 1.84 (1H, m), 2.55 (2H, m), 3.72 (1H, q, J=7 Hz), 4.28 (1H, m), 4.49 (1H, d, J=12 Hz), 4.55 (1H, d, J=12 Hz), 4.97 (1H, brd, J=8 Hz), 7.21-7.40 (5H, m);

35 MASS (ES-): m/e 406.

Preparation 13

To a stirred solution of N-tert-butoxycarbonyl-(R)-proline (50 g) in N,N-dimethylformamide (250 ml), cesium carbonate (37.8 g) was added portionwise under ice-cooling in an ice bath. The ice bath was removed and the suspension was stirred at ambient temperature for 1.5 hours. To the suspension benzyl bromide (40.9 g) was added under ice-cooling and the mixture was stirred at ambient temperature for two and half an hour. To this mixture, water (250 ml) was added under ice-cooling and the mixture was extracted with ethyl acetate (1500 ml), and washed with water (250 ml, 3 times) and brine (250 ml). The organic layer was dried over anhydrous sodium sulfate, filtered and the filtrate was concentrated in vacuo to give crude Compound (13) (N-tert-butoxycarbonyl-(R)-proline benzyl ester, 87.3 g) as a colorless oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.35 (6H, s), 1.46 (3H, s), 1.76-2.04 (3H, m), 2.07-2.31 (1H, m), 3.31-3.61 (2H, m), 4.26 (0.6H, dd, J=8.0, 3.6 Hz), 4.40 (0.4H, dd, J=8.4, 2.4 Hz), 5.04-5.30 (2H, m), 7.25-7.40 (5H, m);

MASS (ES<sup>+</sup>): m/e 306.13 (M+1).

Preparation 14

To the Compound (13) (114 mg), 4N hydrogen chloride in ethyl acetate (50 ml) was added at ambient temperature and the mixture was stirred at ambient temperature for 2 hours. The mixture was concentrated in vacuo and the residual hydrogen chloride was removed azeotropically with ethyl acetate 4 times.

The residual amorphous solid was dissolved in N,N-dimethylformamide (3 ml), and to the solution were added O-benzyl-N-tert-butoxycarbonyltyrosine (146 mg), 1-ethyl-3-(3'-N,N-dimethylaminopropyl)carbodiimide (63.8 mg) and 1-hydroxybenzotriazole (55.5 mg) under ice-cooling. The mixture was stirred at ambient temperature for 1.5 hours. The mixture was diluted with ethyl acetate (300 ml) and washed with 5% aqueous potassium hydrogensulfate solution (200 ml, 4 times), saturated aqueous sodium bicarbonate solution (300 ml, twice) and brine (300 ml). The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residue was purified by flash chromatography eluted with ethyl

acetate-hexane (1:1 v/v) to give Compound (14) (201 mg) as a colorless amorphous solid.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 7.45-7.25 (10H, m), 7.11 (2H, d,  $J=8$  Hz), 6.87 (2H, d,  $J=8$  Hz), 5.37 (1H, brd,  $J=8.4$  Hz), 5.24-4.95 (2H, m), 4.64-4.52 (1H, m), 4.31 (1H, dd,  $J=7.3$ , 4.8 Hz), 3.55-3.45 (2H, m), 3.00 (1H, dd,  $J=12.8$ , 5.6 Hz), 2.86 (1H, dd,  $J=12.8$ , 9.6 Hz), 2.70-2.55 (1H, m), 1.92-1.70 (2H, m), 1.60 (1H, m), 1.43 (9H, s);  
MASS (ES+):  $m/e$  559.36 ( $M+1$ ).

#### Preparation 15

10 To the Compound (14) (6.21 g) was added 4N hydrogen chloride in ethyl acetate (100 ml) under ice-cooling and the mixture was stirred at ambient temperature for one hour. The mixture was concentrated in vacuo and the residual hydrogen chloride was removed 4 times azeotropically with ethyl acetate.

15 The residual amorphous solid was dissolved in  $N,N$ -dimethylformamide (60 ml), then Compound 1 (2.42 g), PyBOP® (6.36 g) (Nova biochem, benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate) and  $N,N$ -diisopropylethylamine (4.74 g) were added to this solution, and the resulting mixture was stirred at ambient  
20 temperature for 16 hours. The volatiles were removed in vacuo and the residue was extracted with ethyl acetate (500 ml).

The organic layer was washed with aqueous 5% potassium hydrogensulfate solution (100 ml, 4 times), saturated aqueous sodium bicarbonate solution (100 ml, 4 times), water (100 ml) and brine (100  
25 ml). The organic layer was separated, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residue was purified by flash chromatography (eluting with ethyl acetate/hexane = 2:1 v/v) to give Compound (15) (5.10 g) as an amorphous solid.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 7.55-7.20 (10H, m), 7.10 (2H, d,  $J=7.6$  Hz), 7.00-6.73 (3H, m), 5.20-4.96 (3H, m), 4.94-4.80 (1H, m), 4.49-4.30 (1H, m), 3.61-3.44 (2H, m), 3.00 (1H, dd,  $J=13.0$ , 5.4 Hz), 2.86 (1H, dd,  $J=13.0$ , 8.8 Hz), 2.75-2.60 (1H, m), 2.06-1.35 (5H, m), 1.43 (9H, s), 0.80 (3H, t,  $J=6.3$  Hz);  
MASS (ES+):  $m/e$  658.43 ( $M+1$ ).

#### Preparation 16

35 To the Compound (15) (5.59 g) was added 4N hydrogen chloride in

ethyl acetate (50 ml) under ice-cooling and the mixture was stirred at ambient temperature for 1 hour. The mixture was concentrated in vacuo and the residual hydrogen chloride was removed 4 times azeotropically with ethyl acetate.

5       The residue was dissolved in dichloromethane (50 ml) and to this solution was added Compound b (3.14 g), PyBOP® (4.86 g) and N,N-diisopropylethylamine (3.62 g) under ice-cooling, and the resulting mixture was stirred at ambient temperature for 16 hours. The volatiles were removed in vacuo and the residue was extracted with  
10 ethyl acetate (500 ml). The organic layer was washed with 5% aqueous potassium hydrogensulfate solution (200 ml, 4 times), saturated aqueous sodium bicarbonate solution (200 ml, twice), water (200ml, twice) and brine (100 ml). The residue was purified by flash chromatography (eluting with ethyl acetate/hexane = 2:1 v/v) to give  
15 Compound (16) (5.2 g) as a colorless amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 8.10-7.98 (2H, m), 7.60-7.22 (13H, m), 7.14-6.77 (5H, m), 6.69 (1H, brd, J=6.7 Hz), 5.18-4.95 (5H, m), 4.93-4.83 (1H, m), 4.39-4.32 (1H, m), 4.31 (2H, t, J=6.6 Hz), 4.12-4.02 (1H, m), 3.61-3.49 (2H, m), 3.03-2.85 (2H, m), 2.82-2.70 (1H, m), 2.36-2.19  
20 (1H, m), 1.98-1.38 (10H, m), 1.50 (3H, s), 1.44 (9H, s), 0.72 (3H, t, J=7.3 Hz);

MASS (ES+): m/e 891.49 (M).

#### Preparation 17

A solution of the Compound (16) (5.43 g) in ethyl acetate (110  
25 ml) was hydrogenated in the presence of palladium hydroxide and 20 wt% Pd (dry basis) on carbon (Pearlman's catalyst) (540 mg) for 4 hours under atmosphere pressure. The catalyst was filtered off through a pad of Celite® and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography eluting with  
30 chloroform/methanol = 10:1 v/v to give Compound (17) as a colorless amorphous (4.96 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.0 Hz), 1.44 (9H, s), 1.30-2.00 (13H, m), 2.06-2.19 (1H, m), 2.64-2.77 (1H, m), 2.95 (2H, brd, J=6.6 Hz), 3.55-3.69 (1H, m), 3.94-4.07 (1H, m), 4.25-4.38 (3H, m),  
35 4.87 (1H, m), 5.05 (2H, s), 6.82 (1H, s), 6.87 (2H, d, J=8.5 Hz), 7.11 (2H, d, J=8.5 Hz), 7.20 (1H, brd, J=8.8 Hz), 7.27-7.60 (8H, m), 7.99-

8.07 (2H, m);

MASS (ES+): m/e 801.47 (M+1).

#### Preparation 18

To the Compound (17) (4.96 g) was added 4N hydrogen chloride in  
5 ethyl acetate (60 ml) under ice-cooling and the mixture was stirred at  
ambient temperature for 3 hours. The solvent was concentrated in  
vacuo and the residual hydrogen chloride was removed azeotropically  
with ethyl acetate (100 ml, 4 times). The residue was dried in vacuo  
to give Compound (18) (4.64 g) as a pale brown amorphous solid. The  
10 obtained compound was used in the Preparation 75.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60-0.82 (3H, m), 1.25-2.20 (15H, m),  
2.74-3.07 (4H, m), 3.63-3.79 (1H, m), 4.13-4.38 (3H, m), 4.82-4.95 (1H,  
m), 4.99 (2H, s), 6.83 (2H, d, J=7.3 Hz), 7.10 (2H, d, J=7.3 Hz),  
7.20-7.54 (8H, m), 7.51 (1H, t, J=8.1 Hz), 7.57-7.70 (1H, m), 7.99 (2H,  
15 d, J=7.0 Hz), 8.07-8.40 (2H, m);

MASS (ES+): m/e 701.36 (free+1).

#### Preparation 19

The Compound (13) (10.0 g) was dissolved in ethyl acetate (60  
ml) and the mixture was stirred for 4 hours at ambient temperature.  
20 The solvent was evaporated and the residual solvent was removed  
azeotropically with toluene. The residue was washed with ethyl  
acetate and dried to give D-proline benzyl ester hydrochloride  
(hereinafter Compound 19).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.92 (2H, m), 2.01 (1H, m), 2.28 (1H, m),  
25 3.22 (1H, m), 4.44 (1H, dd, J=8, 7 Hz), 5.23 (1H, d, J=12 Hz), 5.26  
(1H, d, J=12 Hz), 7.23-7.47 (5H, m);

MASS (ES+): m/e 206.

#### Preparation 20

N-t-Butoxycarbonyl O-methyl-L-tyrosine (3.62 g) was dissolved  
30 in dichloromethane (40 ml), then Compound 19 (2.82 g),  
hydroxybenzotriazol (1.73 g) and a solution of 1-ethyl-3-(3'-  
dimethylaminopropyl)carbodiimide hydrogen chloride (1.99 g) in  
dichloromethane (5 ml) were added to the mixture and the mixture was  
stirred for 14 hours at ambient temperature. The reaction mixture was  
35 added to 10% aqueous solution of citric acid (50 ml) then 5% aqueous  
solution of potassium hydrogensulfate (50 ml) was added to the mixture.

The mixture was washed with saturated aqueous sodium bicarbonate solution (50 ml) and saturated aqueous sodium chloride solution (50 ml) then dried over magnesium sulfate, and evaporated to dryness to give a crude compound. The crude compound was purified by flash

5 column chromatography (Silica gel 60, Spherical, 120 g, eluent: ethyl acetate : hexane = 1:2 to 1:1) to give Compound (20) (5.55 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.43 (3x3H, s), 1.55 (1H, m), 1.74-2.00 (3H, m), 2.69 (1H, m), 2.87 (1H, dd, J=13.9 Hz), 3.00 (1H, dd, J=13, 5 Hz), 3.54 (1H, m), 4.36 (1H, dd, J=8, 4 Hz), 4.60 (1H, m), 5.11 (1H, d, J=12.5 Hz), 5.19 (1H, d, J=12.5 Hz), 5.37 (1H, d, J=9 Hz), 6.79 (2x1H, d, J=8.5 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.28-7.40 (5H, m);

MASS (ES<sup>+</sup>): m/e 483.

#### Preparation 21

The Compound (20) (5.50 g) was dissolved in ethyl acetate (30 ml) and a cold solution of 4N hydrogen chloride in ethyl acetate (50 ml) was added to the mixture and stirred for 2.5 hours at ambient temperature. The mixture was evaporated to dryness to give Compound (21) (4.97 g) as a white foam.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.60 (1H, m), 1.70-1.87 (2H, m), 1.97 (1H, m), 2.80 (1H, m), 2.91 (1H, dd, J=13, 8 Hz), 3.06 (1H, dd, J=13, 6 Hz), 3.58 (1H, m), 4.30 (1H, dd, J=9, 3 Hz), 4.36 (1H, m), 5.08 (1H, d, J=13 Hz), 5.19 (1H, d, J=13 Hz), 6.90 (2x1H, d, J=8 Hz), 7.14 (2x1H, d, J=8 Hz), 7.30-7.44 (5H, m), 8.34 (2H, br);

MS (ES<sup>+</sup>): m/e 383.

#### 25 Preparation 22

The Compound (21) (4.89 g) was dissolved in dichloromethane (40 ml) and Compound a (4.31 g), benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (6.68 g) and N-ethyldiisopropylamine (4.83 g) were added to the solution, and the mixture was stirred for 15 hours at ambient temperature. The mixture was diluted with chloroform (40 ml), washed with 5% aqueous solution of potassium hydrogensulfate (50 ml), saturated aqueous sodium bicarbonate solution (50 ml) and saturated aqueous sodium chloride solution (50 ml), dried over sodium sulfate and evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60N, Spherical, 120 g, eluent: ethyl

acetate : hexane = 1:2 to 1:1) to give Compound (22) (5.70 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 1.41 (3H, s), 1.44 (9H, s), 1.58 (1H, m), 1.76-2.06 (5H, m), 2.75 (1H, m), 2.89 (1H, dd, J=13, 9 Hz), 3.02 (1H, dd, J=13, 5 Hz), 3.56 (1H, m), 3.77 (3H, s), 4.38 (1H, dd, J=8, 4 Hz), 4.91 (1H, ddd, J=9, 8.5, 5 Hz), 5.11 (1H, d, J=12.5 Hz), 5.15 (1H, d, J=12.5 Hz), 6.80 (2H, d, J=8.5 Hz), 6.84 (1H, d, J=8.5 Hz), 7.13 (2H, d, J=8.5 Hz), 7.28-7.40 (5H, m);

MASS (ES<sup>+</sup>): m/e 582.

#### Preparation 23

10        The Compound (22) (5.31 g) was dissolved in ethyl acetate (30 ml) and cold solution of 4N hydrogen chloride in ethyl acetate (50 ml) was added to the mixture and stirred for 1 hour at ambient temperature. The mixture was evaporated to dryness to give Compound (23) (5.31 g) as a white foam.

15        <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.75 (3H, d, J=7 Hz), 1.33 (3H, s), 1.63-2.30 (6H, m), 2.84 (1H, dd, J=13, 10 Hz), 2.93 (1H, dd, J=13, 5 Hz), 3.51 (1H, m), 3.74 (1H, m), 4.34 (1H, dd, J=9, 4 Hz), 4.80 (1H, ddd, J=9 Hz), 7.20 (2x1H, d, J=9 Hz), 7.29-7.45 (1H, m), 8.03 (2H, brs), 8.64 (1H, d, J=9 Hz);

20        MS (ES<sup>+</sup>): m/e 482.

#### Preparation 24

      The Compound (23) (5.26 g) was dissolved in dichloromethane (30 ml) and a solution of Compound (5) (3.57g) in dichloromethane (50 ml), benzotriazol-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (6.34 g) and N-ethyldiisopropylamine (4.2 g) were added to the solution, and the mixture was stirred for 12 hours at ambient temperature. The mixture was diluted with chloroform (80 ml), washed with 5% aqueous solution of potassium hydrogensulfate (100 ml), saturated aqueous sodium bicarbonate solution (100 ml) and saturated aqueous sodium chloride solution (100 ml), dried over sodium sulfate and evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60N, Spherical, 150 g, eluent: ethyl acetate : hexane = 1:1 to 1:2) to give Compound (24) (5.76 g).

35        <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, t, J=7.3 Hz), 1.43 (3H, s), 1.44 (3x3H, s), 1.47-2.36 (12H, m), 2.84 (1H, m), 2.92 (1H, dd, J=13, 9.5

Hz), 2.98 (1H, dd, J=13, 5.5 Hz), 3.58 (1H, m), 3.77 (3H, s), 4.08 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.39 (1H, dd, J=8, 4 Hz), 4.91 (1H, m), 5.12 (1H, m), 5.13 (2H, s), 6.70 (1H, brd, J=9 Hz), 6.80 (2x1H, d, J=8.5 Hz), 7.01 (1H, s), 7.10 (2x1H, d, J=8.5 Hz), 7.28-7.36 (5H, m),  
5 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, dd, J=7.5, 7.5 Hz), 8.03 (2x1H, d, J=7.5 Hz);

MASS (ES-): m/e 813.

#### Preparation 25

Compound (25) was obtained in a manner similar to Preparation  
10 17 except that Compound (24) was used instead of the Compound (16) and palladium on carbon was used instead of the Pearlman's catalyst.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.5 Hz), 1.38-2.36 (12H, m), 1.44 (9+3H, s), 2.79 (1H, m), 2.90-3.02 (2H, m), 3.67 (1H, m), 3.77 (3H, s), 4.02 (1H, m), 4.26-4.42 (3H, m), 4.88 (1H, m), 5.20 (1H, m),  
15 6.81 (2x1H, d, J=8.5 Hz), 6.83 (1H, brs), 7.12 (2x1H, d, J=8.5 Hz), 7.24 (1H, d, J=8 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dd, J=7.5, 7.5 Hz), 8.04 (2x1H, d, J=7.5 Hz);

MASS (ES-): m/e 723.

#### Preparation 26

20 Compound (26) was obtained in a manner similar to Preparation 18 except that trifluoroacetic acid was used instead of 4N hydrogen chloride. The obtained compound was used in Preparation 78.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.54 (3x1/3H, t, J=7.3 Hz), 0.66 (3x2/3H, t, J=7.3 Hz), 1.31 (3x1/3H, s), 1.35 (3x2/3H, s), 1.44 (2H, m), 1.60-  
25 2.20 (10H, m), 2.70-2.98 (2H, m), 3.18 (1H, m), 3.36 (1H, m), 3.67 (3x1/3H, s), 3.69 (3x2/3H, s), 4.12 (1x2/3H, dd, J=9.3 Hz), 4.26 (2H, t, J=6 Hz), 4.41 (1H, m), 4.77 (1H, m), 4.84 (1x1/3H, dd, J=9.3 Hz), 6.78 (2x1/3H, d, J=9 Hz), 6.81 (2x2/3H, d, J=9 Hz), 7.10-7.30 (3H, m), 7.48-7.60 (2H, m), 7.68 (1H, m), 7.88-8.17 (5H, m);

30 MASS (ES+): m/e 625.

#### Preparation 27

Compound (27) was obtained in a manner similar to Preparation (14).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.42 (9H, s), 1.50-1.68 (1H, m), 1.80-2.03  
35 (3H, m), 2.71-2.84 (1H, m), 2.92 (1H, dd, J=13.2, 8.7 Hz), 3.00 (1H, dd, J=13.2, 6.1 Hz), 3.53-3.65 (1H, m), 4.36 (1H, dd, J=7.7, 3.6 Hz),

4.62 (1H, dt, J=8.5, 5.9 Hz), 5.10 (1H, d, J=12.5 Hz), 5.20 (1H, d, J=12.5 Hz), 5.34 (1H, d, J=8.0 Hz), 6.88-7.03 (2H, m), 7.17 (2H, dd, J=8.5, 5.5 Hz), 7.30-7.40 (5H, m);  
MASS (ES+): m/e 471.37 (M+1).

5 Preparation 28

Compound (28) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.6 Hz), 1.39 (3H, s), 1.43 (9H, s), 1.76-2.03 (6H, m), 2.74-2.87 (1H, m), 2.95 (1H, dd, J=13.2 and 9.1 Hz), 3.03 (1H, dd, J=13.2 and 4.8 Hz), 3.51-3.66 (1H, m), 4.38 (1H, dd, J=8.1, 3.7 Hz), 4.87-4.98 (1H, m), 4.98-5.20 (3H, m), 6.81-7.02 (3H, m), 7.15-7.23 (2H, m), 7.28-7.41 (5H, m);  
MASS (ES+): m/e 570.42 (M+1).

Preparation 29

15 Compound (29) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.61 (0.6H, t, J=7.3 Hz), 0.72 (2.4H, t, J=7.3 Hz), 1.39-2.08 (11H, m), 1.43 (9H, s), 1.48 (3H, s), 2.13-2.33 (1H, m), 2.83-2.99 (1H, m), 2.98 (2H, d, J=7.0 Hz), 3.51-3.70 (1H, m), 20 3.92-4.15 (1H, m), 4.31 (2H, t, J=5.9 Hz), 4.39 (1H, dd, J=7.3, 3.2 Hz), 4.92 (1H, q, J=7.3 Hz), 5.02-5.15 (2H, m), 5.17 (1H, s), 6.72 (1H, brs), 6.83-7.05 (3H, m), 7.16 (2H, dd, J=8.4, 5.5 Hz), 7.27-7.38 (5H, m), 7.39-7.47 (2H, m), 7.51-7.60 (1H, m), 8.03 (2H, d, J=7.3 Hz);  
MASS (ES+): m/e 803.55 (M+1).

25 Preparation 30

Compound (30) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.4 Hz), 1.17-2.02 (11H, m), 1.45 (12H, s), 2.11-2.25 (1H, m), 2.79-3.10 (3H, m), 3.64-3.79 (1H, m), 30 4.26-4.42 (3H, m), 4.92 (1H, q, J=7.6 Hz), 5.23 (1H, brs), 6.79 (1H, brs), 6.97 (2H, t, J=8.5 Hz), 7.19 (2H, dd, J=8.5, 5.2 Hz), 7.30 (1H, d, J=8.3 Hz), 7.39-7.48 (2H, m), 7.52-7.62 (1H, m), 8.04 (2H, d, J=8.5 Hz);  
MASS (ES+): m/e 713.54 (M+1).

35 Preparation 31

Compound (31) was obtained in a manner similar to Preparation

18. The obtained compound was used in Preparation 81.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, t, J=7.4 Hz), 1.38 (3H, s), 1.51-2.16 (12H, m), 2.83-3.15 (3H, m), 3.68-3.83 (1H, m), 4.18-4.37 (4H, m), 4.86-4.98 (1H, m), 6.92 (2H, t, J=8.5 Hz), 7.17 (2H, dd, J=8.5, 5.8 Hz), 7.39 (2H, t, J=7.7 Hz), 7.53 (1H, t, J=7.6 Hz), 7.67 (1H, brs), 7.99 (2H, d, J=7.3 Hz), 8.13-8.39 (3H, m);

MASS (ES<sup>+</sup>): m/e 613.49 (M+1, free).

Preparation 32

Compound (32) was obtained in a manner similar to Preparation 14.

Preparation 33

Compound (33) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.31-1.54 (9H, m), 1.55-1.99 (8H, m), 2.01-2.42 (3H, m), 2.52-2.63 (1H, m), 2.80-2.96 (1H, m), 3.03-3.14 (1H, m), 3.44-3.60 (2H, m), 4.31-4.38 (1H, m), 4.68-4.86 (1H, m), 4.94 (1H, dt, J=9.9, 5.1 Hz), 5.05-5.20 (2H, m), 7.08 (1H, d, J=8.1 Hz), 7.16-7.39 (10H, m);

MASS (ES<sup>+</sup>): m/e 564.38 (M+1).

20 Preparation 34

Compound (34) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.32-2.06 (20H, m), 1.44 (9H, s), 2.09-2.30 (2H, m), 2.64-2.74 (1H, m), 2.88-3.08 (1H, m), 3.53-3.62 (2H, m), 3.98-4.08 (1H, m), 4.27-4.37 (4H, m), 4.85-4.95 (1H, m), 5.07-5.21 (3H, m), 6.63 (1H, s), 7.12-7.37 (6H, m), 7.42 (2H, dd, J=8.1, 6.9 Hz), 7.55 (1H, dd, J=6.9, 6.9 Hz), 8.03 (2H, d, J=8.1 Hz);

MASS (ES<sup>+</sup>): m/e 797.50 (M+1).

Preparation 35

30 Compound (35) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.16-2.12 (15H, m), 1.44 (9H, s), 2.24-2.41 (1H, m), 2.62-2.76 (1H, m), 2.90-3.09 (2H, m), 3.47-3.50 (1H, m), 3.65-3.77 (1H, m), 4.01-4.11 (2H, m), 4.24-4.38 (4H, m), 4.74-4.84 (1H, m), 5.56-5.64 (1H, m), 6.84-6.92 (1H, m), 7.16-7.31 (6H, m), 7.43 (2H, dd, J=7.8, 6.9 Hz), 7.56 (1H, dd, J=7.8, 7.8 Hz), 8.02 (2H, d, J=6.9

Hz);

MASS (ES+): m/e 707.45 (M+1).

Preparation 36

Compound (36) was obtained in a manner similar to Preparation

5 18. The obtained compound was used in Preparation 84.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.34-2.27 (19H, m), 2.79-3.19 (3H, m),  
3.48-3.78 (1H, m), 3.95-4.13 (1H, m), 4.14-4.47 (3H, m), 4.82-5.00 (1H,  
m), 7.11-7.32 (5H, m), 7.34-7.46 (2H, m), 7.48-7.58 (1H, m), 7.62-7.84  
(1H, brs), 7.95-8.06 (2H, m), 8.06-8.36 (2H, brs), 8.63-9.02 (1H,

10 brs);

MASS (ES+): m/e 607.42 (M+1).

Preparation 37

Compound (37) was obtained in a manner similar to Preparation

19.

15 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.31 (3H, s), 1.40 (6H, s), 1.56-1.80 (3H,  
m), 1.84-2.11 (2H, m), 2.92-3.13 (2H, m), 3.57-3.70 (1H, m), 4.36-4.42  
(1H, m), 4.62-4.72 (1H, m), 5.04-5.34 (3H, m), 7.11-7.51 (7H, m),  
7.54-7.60 (3H, m);

MASS (ES+): m/e 478.40 (M+1).

20 Preparation 38

Compound (38) was obtained in a manner similar to Preparation

15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.800 (3H, t, J=7.5 Hz), 1.36 (3H, s), 1.39  
(3H, s), 1.43 (6H, s), 1.52-1.62 (2H, m), 1.67-2.06 (4H, m), 2.83-3.16  
25 (2H, m), 3.50-3.70 (2H, m), 4.36-4.42 (1H, m), 4.86-5.04 (2H, m),  
5.06-5.21 (2H, m), 6.87 (1H, d, J=9.0 Hz), 7.29-7.48 (6H, m), 7.53-  
7.59 (3H, m);

MASS (ES+): m/e 577.40 (M+1).

Preparation 39

30 Compound (39) was obtained in a manner similar to Preparation

16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.740 (3H, t, J=7.2 Hz), 1.30-2.29 (11H, m),  
1.34 (3H, s), 1.44 (9H, s), 2.86-3.18 (3H, m), 3.51-3.72 (2H, m),  
3.99-4.08 (1H, m), 4.27-4.42 (3H, m), 4.96-5.04 (1H, m), 5.06-5.19 (3H,  
35 m), 6.82 (1H, s), 7.12-7.17 (1H, m), 7.28-7.37 (6H, m), 7.39-7.47 (3H,  
m), 7.52-7.61 (3H, m), 8.00-8.05 (2H, m);

MASS (ES+): m/e 810.59 (M+1).

Preparation 40

Compound (40) was obtained in a manner similar to Preparation 17.

5  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.731 (3H, t,  $J=7.2$  Hz), 1.31-2.22 (13H, m), 1.40 (3H, s), 1.44 (9H, s), 2.91-3.23 (3H, m), 3.80-3.94 (1H, m), 3.99-4.13 (1H, m), 4.23-4.43 (3H, m), 4.86-5.00 (1H, m), 5.48-5.60 (1H, m), 6.76 (1H, s), 7.25-7.31 (1H, m), 7.31-7.38 (2H, m), 7.40-7.47 (2H, m), 7.52-7.61 (3H, m), 8.00-8.06 (2H, m);

10 MASS (ES+): m/e 720.38 (M+1).

Preparation 41

Compound (41) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation C5.

15  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.59-0.73 (3H, m), 1.33 (3H, s), 1.52-2.17 (12H, m), 2.92-3.27 (3H, m), 3.70-3.83 (1H, m), 4.14-4.40 (4H, m), 4.90-5.02 (1H, m), 7.31-7.45 (5H, m), 7.49-7.59 (3H, m), 7.59-7.71 (1H, brs), 7.93-8.11 (5H, m);

MASS (ES+): m/e 620.33 (M+1).

Preparation 42

20 Compound (42) was obtained in a manner similar to Preparation 19.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.39 (3H, t,  $J=7.2$  Hz), 1.43 (9H, s), 1.46-1.63 (1H, m), 1.76-2.00 (3H, m), 2.62-2.72 (1H, m), 2.82-2.92 (1H, m), 2.94-3.04 (1H, m), 3.48-3.58 (1H, m), 3.98 (2H, q,  $J=7.2$  Hz), 4.32-25 4.42 (1H, m), 4.53-4.64 (1H, m), 5.10 (1H, d,  $J=12.6$  Hz), 5.20 (1H, d,  $J=12.6$  Hz), 5.37 (1H, d,  $J=8.7$  Hz), 6.78 (2H, d,  $J=8.7$  Hz), 7.11 (2H, d,  $J=8.7$  Hz), 7.28-7.39 (5H, m);

MASS (ES+): m/e 497.34 (M+1).

Preparation 43

30 Compound (43) was obtained in a manner similar to Preparation 15.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.80 (3H, t,  $J=7.5$  Hz), 1.39 (3H, t,  $J=7.2$  Hz), 1.40 (3H, s), 1.43 (9H, s), 1.50-1.64 (1H, m), 1.75-2.05 (5H, m), 2.67-2.79 (1H, m), 2.81-2.93 (1H, m), 2.94-3.05 (1H, m), 3.50-3.62 (1H, 35 m), 3.98 (2H, q,  $J=7.2$  Hz), 4.37 (1H, dd,  $J=7.5$ , 3.3 Hz), 4.90 (1H, dt,  $J=9.6$ , 5.1 Hz), 5.10 (1H, d,  $J=12.3$  Hz), 5.15 (1H, d,  $J=12.3$  Hz),

6.57-6.97 (1H, m), 6.78 (2H, d, J=8.4 Hz), 7.11 (2H, d, J=8.4 Hz),  
7.29-7.39 (5H, m);  
MASS (ES+): m/e 596.51 (M+1).

Preparation 44

- 5           Compound (44) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.74 (3H, t, J=7.5 Hz), 1.40 (3H, t, J=7.2 Hz), 1.45 (9H, s), 1.47-1.99 (11H, m), 1.50 (3H, s), 2.18-2.29 (1H, m), 2.76-3.00 (2H, m), 3.44-3.65 (2H, m), 3.99 (2H, q, J=7.2 Hz), 4.03-  
10 4.13 (1H, m), 4.33 (2H, t, J=6.3 Hz), 4.40 (1H, dd, J=7.2, 3.6 Hz), 4.83-4.94 (1H, m), 5.10-5.19 (3H, m), 6.79 (2H, d, J=8.4 Hz), 6.92-7.04 (1H, m), 7.10 (2H, d, J=8.4 Hz), 7.29-7.39 (6H, m), 7.40-7.48 (2H, m), 7.52-7.60 (1H, m), 8.01-8.07 (2H, m);  
MASS (ES+): m/e 829.61 (M+1).

- 15   Preparation 45

Compound (45) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7.5 Hz), 1.40 (3H, t, J=7.2 Hz), 1.44 (12H, s), 1.57-2.72 (11H, m), 2.65-3.03 (3H, m), 3.58-3.83  
20 (2H, m), 3.99 (2H, q, J=7.2 Hz), 4.04-4.15 (1H, m), 4.23-4.39 (3H, m), 4.75-4.88 (1H, m), 5.53-5.63 (1H, m), 6.79 (2H, d, J=8.7 Hz), 7.09 (2H, d, J=8.7 Hz), 7.13-7.21 (1H, m), 7.39-7.48 (2H, m), 7.52-7.59 (1H, m), 8.00-8.06 (2H, m);  
MASS (ES+): m/e 739.58 (M+1).

- 25   Preparation 46

Compound (46) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 91.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, t, J=6.9 Hz), 1.34 (3H, s), 1.38 (3H, t, J=7.2 Hz), 1.54-2.13 (12H, m), 2.80-3.18 (3H, m), 3.64-3.78  
30 (1H, m), 3.36 (2H, q, J=7.2 Hz), 4.14-4.38 (4H, m), 4.77-4.89 (1H, m), 6.77 (2H, d, J=8.7 Hz), 7.09 (2H, d, J=8.7 Hz), 7.37-7.48 (2H, m), 7.49-7.57 (1H, m), 7.80-8.22 (6H, m);  
MASS (ES+): m/e 739.58 (free M+1).

Preparation 47

- 35           Compound (47) was purchased from Kokusan Chemical Co., Ltd.

Preparation 48

Fmoc-2-fluorophenylalanine (available from Oakwood Products, Inc.), 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide hydrochloride (1.29 g) and 1-hydroxybenzotriazole (911 mg) were added to dichloroethane (30 ml), and the mixture was sonicated to give a homogeneous mixture. To this mixture, Compound (47) (1.05 g) in dichloromethane (10 ml) was added and stirred at ambient temperature for 1.3 hours. The reaction mixture was added to 10% aqueous citric acid (30 ml), then the organic layer was collected. To the aqueous layer was added water (30 ml), then the mixture was extracted with chloroform (50 ml). The organic layer and the chloroform extract were combined, washed with saturated aqueous sodium bicarbonate solution (30 ml) and brine (30 ml), dried over magnesium sulfate, and the solvent was evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60, Spherical, 40 g, eluted with ethyl acetate/hexane = 1:2 to 1:1 v/v) to give Compound (48) (3.29 g) as a white foam.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.43 (9x4/5H, s), 1.51 (9x1/5H, s), 1.63-2.30 (4H, m), 3.00-3.14 (2H, m), 3.20 (1H, m), 3.70 (1H, m), 4.04-4.42 (4H, m), 4.58 (1x1/5H, m), 4.82 (1x4/5H, m), 5.48 (1x4/5H, d,  $J=8$  Hz), 5.71 (1x1/5H, d,  $J=8$  Hz), 6.95-7.08 (2H, m), 7.11-7.62 (8H, m), 7.71-7.80 (2H, m);

MASS (ES<sup>+</sup>): m/e 559.

#### Preparation 49

The Compound (48) (3.25 g) was dissolved in acetonitrile (15 ml), N,N-diethylamine (15 ml) was added to the mixture and stirred for 1 hour at ambient temperature. The solvent was evaporated and the residual solvent was removed azeotropically with toluene to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60, Spherical, 40-50  $\mu\text{m}$ , eluted with methanol/chloroform = 1:40 v/v) to give Compound (49) (1.52 g) as a white foam.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.46 (9x5/6H, s), 1.47 (9x1/6H, s), 1.56-2.25 (4H, m), 2.79 (1x1/6H, dd,  $J=13$ , 8 Hz), 2.83 (1x5/6H, dd,  $J=13$ , 8 Hz), 2.94 (1x5/6H, dd,  $J=13$ , 7 Hz), 3.10 (1x1/6H, dd,  $J=13$ , 5 Hz), 3.19 (1H, m), 3.62 (1H, m), 3.83 (1H, d,  $J=8$ , 7 Hz), 4.28 (1x5/6H, dd,  $J=8$ , 4 Hz), 4.60 (1x1/6H, dd,  $J=8$ , 3 Hz), 6.98-7.12 (2H, m), 7.17-7.28 (2H,

m);

MASS (ES+): m/e 337.

#### Preparation 50

The Compound (49) (1.51 g) was dissolved in dichloromethane (20 ml) and 2(S)-ethyl-2-benzyloxycarbonylaminopropionic acid (1.13 g), PyBroP® (2.3 g) and N-ethyl-N,N-diisopropylamine (696 mg) were added to the solution, and the mixture was stirred for 5 hours at ambient temperature. The mixture was washed with 10% aqueous solution of citric acid (30 ml), saturated aqueous sodium bicarbonate solution (30 ml) and saturated aqueous sodium chloride solution (30 ml), dried over magnesium sulfate and the solvent was evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60N, Spherical, 40 g, eluent: ethyl acetate : hexane = 1:2 to 1:1) to give Compound (50) (1.54 g).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60 (3x1/4H, t, J=7 Hz), 0.75 (3x3/4H, t, J=7.3 Hz), 1.33-2.30 (18H, m), 2.98-3.32 (3H, m), 3.50-3.80 (1H, m), 4.25 (1x3/4H, dd, J=8, 4 Hz), 4.67-5.10 (3+1/4H, m), 5.53 (1x1/4H, br), 5.78 (1x3/4H, br), 6.57 (1x1/4H, br), 6.73 (1x3/4H, brd, J=8 Hz), 6.94-7.07 (2H, m), 7.11-7.24 (2H, m), 7.28-7.39 (5H, m);

MASS (ES+): m/e 570.

#### Preparation 51

The Compound (50) (1.52 g) was dissolved in methanol and 10% palladium on carbon (150 mg) suspended in water (1 ml) was added to the solution and stirred for 2 hours at ambient temperature, 3 atm. The catalyst was filtered off through a pad of Celite®, the solvent was evaporated, then the residual solvent was removed azeotropically with toluene to give Compound (51).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.42 (3x1/3H, t, J=7.4 Hz), 0.72 (3x2/3H, t, J=7.5 Hz), 1.19 (3x1/3H, s), 1.26 (3x2/3H, s), 1.43 (9x2/3H, s), 1.51 (9x1/3H, s), 1.69-2.30 (6H, m), 2.99-3.30 (3H, m), 3.56-3.77 (1H, m), 4.25 (1x2/3H, dd, J=8 and 4 Hz), 4.71 (1x1/3H, m), 5.02 (1x2/3H, m), 5.04 (1x1/3H, m), 6.93-7.08 (2H, m), 7.12-7.25 (2H, m);

MASS (ES+): m/e 436.

#### Preparation 52

The Compound (51) (1.15 g) was dissolved in dichloromethane (15 ml) and a solution of Compound (5) (1.02 g) in dichloromethane (10 ml),

benzotriazole-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (1.65 g) and N-ethyl-N,N-diisopropylamine (751 mg) were added to the solution, and the mixture was stirred for 14 hours at ambient temperature. The mixture was washed with 10% aqueous solution of citric acid (30 ml), saturated aqueous sodium bicarbonate solution (30 ml) and saturated aqueous sodium chloride solution (30 ml), dried over sodium sulfate and the solvent was evaporated to give a crude compound. The crude compound was purified by flash column chromatography (Silica gel 60, Spherical, 50 g, eluent: ethyl acetate : hexane = 1:1 to 2:1) to give Compound (52) (1.74 g) as a white foam.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60 (3x1/3H, t, J=7.5 Hz), 0.71 (3x2/3H, t, J=7.5 Hz), 1.34-2.44 (12H, m), 1.41 (9x2/3H, s), 1.43 (9x1/3H, s), 1.49 (3x1/3H, s), 1.51 (3x2/3H, s), 3.00-3.12 (2H, m), 3.23-3.76 (2H, m); 4.07 (1H, m), 4.25 (1H, dd, J=8, 4 Hz), 4.31 (2H, t, J=6.5 Hz), 4.67-5.17 (2H, m), 6.54 (1x1/3H, brd, J=8 Hz), 6.70 (1x2/3H, brd, J=8 Hz), 6.93-7.09 (3H, m), 7.10-7.25 (2H, m), 7.43 (2H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dd, J=7.5, 7.5 Hz), 8.03 (2H, d, J=7.5 Hz);

MASS (ES-): m/e 767.

#### Preparation 53

Compound (53) was obtained in a manner similar to Preparation 18 except that trifluoroacetic acid was used instead of 4N hydrogen chloride. The obtained compound was used in Preparation 93.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.62 (3H, t, J=7.3 Hz), 1.20 (3H, s), 1.49-2.15 (12H, m), 2.88-3.10 (2H, m), 3.34 (1H, m), 3.82 (1H, m), 4.07 (1H, m), 4.23-4.38 (3H, m), 4.92 (1H, m), 6.96-7.11 (2H, m), 7.14-7.28 (3H, m), 7.42 (2H, dd, J=7.6, 7.6 Hz), 7.50-7.58 (2H, m), 7.82 (2H, br), 8.01 (2H, d, J=7.6 Hz);

MASS (ES+): m/e 613.

#### Preparation 54

Compound (54) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 96.

#### Preparation 55

Compound (55) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 99.

#### Preparation 56

Compound (56) was obtained in a manner similar to Preparation

16.

Preparation 57

Compound (57) was obtained in a manner similar to Preparation 18 except that trifluoroacetic acid was used instead of 4N hydrogen chloride. The obtained compound was used in Preparation 102.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, t, J=7 Hz), 1.27 (3H, s), 1.49-2.10 (12H, m), 2.85-3.05 (3H, m), 3.70 (1H, m), 4.09 (1H, m), 4.24 (1H, m), 4.27-4.40 (2H, m), 4.83 (1H, m), 7.13-7.34 (5H, m), 7.42 (2x1H, dd, J=8.8 Hz), 7.55 (1H, m), 7.80 (2H, br), 7.89 (1H, s), 8.00 (2x1H, dd, J=8 and 1 Hz);

MASS (ES<sup>+</sup>): m/e 595.

Preparation 58

Compound (58) was obtained in a manner similar to Preparation 18. The obtained compound was used in Preparation 105.

15 Preparation 59

Compound (59) was obtained in a manner similar to Preparation 14.

Preparation 60

The Compound (59) (600 mg) was dissolved in dichloromethane (10 ml), tert-butoxycarbonyl-D-tert-leucine (444 mg), a solution of 1-ethyl-3-(3'-N,N-dimethylaminopropyl)carbodiimide (328 mg) in dichloromethane (2 ml) and hydroxybenzotriazole (285 mg) were added to the solution, and stirred for 15 hours at ambient temperature. The mixture was washed with 10% aqueous solution of citric acid (10 ml), water (20 ml), saturated aqueous sodium bicarbonate solution (20 ml) and saturated aqueous sodium chloride solution (20 ml), dried over sodium sulfate and the solvent was evaporated to give a crude compound as pale yellow oil. The crude compound was purified by flash column chromatography (Kieselgel 60, 30 g, eluent: ethyl acetate : hexane = 1:2 to 1:1) to give Compound (60) (669 mg) as a white foam.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60 (9x1/3H, s), 0.74 (9x2/3H, s), 1.36 (9x1/3H, s), 1.38 (9x2/3H, s), 1.64-2.30 (4H, m), 2.75-2.89 (1+1/3H, m), 2.93 (1x2/3H, dd, J=13.5, 6.5 Hz), 3.16-3.72 (2H, m), 3.84 (1x1/3H, d, J=10 Hz), 3.90 (1x2/3H, d, J=10 Hz), 4.17 (1x2/3H, dd, J=8, 4 Hz), 4.38 (1x1/3H, m), 4.80 (1x2/3H, m), 5.10 (1x1/3H, m), 6.40 (1x1/3H, d, J=10 Hz), 6.47 (1x2/3H, d, J=10 Hz), 7.12-7.30 (5H, m), 8.31 (1x2/3H,

d, J=8 Hz), 8.65 (1x1/3H, d, J=8 Hz);

MASS (ES+): m/e 490.

#### Preparation 61

The Compound (61) (297 mg) was dissolved in dioxane (3 ml) and  
5 cold solution of 4N hydrogen chloride in dioxane (3 ml) was added to  
the mixture and stirred for 12 hours at ambient temperature. The  
mixture was evaporated to dryness to give Compound (61) (250 mg) as a  
white powder.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub> δ): 0.63 (9x1/3H, s), 0.82 (9x2/3H, s), 1.60-  
10 2.30 (4H, m), 2.79-2.92 (1+1/3H, m), 2.97 (2x2/3H, dd, J=13, 7 Hz),  
3.05-3.66 (3H, m), 3.61 (3x2/3H, s), 3.75 (3x1/3H, s), 4.21 (1x2/3H,  
dd, J=8.5, 3.5 Hz), 4.55 (1x1/3H, m), 4.94 (1x2/3H, ddd, J=8, 8, 7 Hz),  
5.14 (1x1/3H, dd, J=8, 4 Hz), 7.12-7.33 (5H, m), 8.10 (2H, br), 8.80  
(1x2/3H, d, J=8 Hz), 9.03 (1x1/3H, d, J=8 Hz);

15 MASS (ES+): m/e 390.

#### Preparation 62

The Compound (61) (227 mg) was dissolved in dichloromethane (3  
ml) and a solution of Compound (12) (217 mg) in dichloromethane (2 ml),  
hydroxybenzotriazole (86.4 mg) and a solution of 1-ethyl-3-(3'-N,N-  
20 dimethylaminopropyl)carbodiimide (99.3 mg) in dichloromethane (3 ml)  
were added to the solution, and the mixture was stirred for 15 hours  
at ambient temperature. The mixture was washed with 10% aqueous  
solution of citric acid (20 ml), saturated aqueous sodium bicarbonate  
solution (20 ml) and saturated aqueous sodium chloride solution (20  
25 ml), dried over sodium sulfate and the solvent was evaporated to give  
a crude compound. The crude compound was purified by preparative thin  
layer chromatography (Merck Art 5717 x 2 plates, eluent: ethyl  
acetate : hexane = 1:1) to give Compound (62) (297 mg) as a white foam.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub> δ): 0.55 (9x1/3H, s), 0.70 (9x2/3H, s), 1.10-  
30 1.90 (10H, m), 1.22 (3H, d, J=7 Hz), 1.36 (9H, s), 1.93-2.33 (2H, m),  
2.40-2.60 (2H, m), 2.71-2.89 (1+1/3H, m), 2.94 (1x2/3H, dd, J=13.7 Hz),  
3.18-3.73 (2H, m), 3.53 (3x2/3H, s), 3.74 (3x1/3H, s), 3.95 (1H, m),  
3.97 (1H, q, J=7 Hz), 4.16 (1x2/3H, dd, J=8.4 Hz), 4.23 (1x1/3H, d,  
J=10 Hz), 4.28 (1x2/3H, d, J=10 Hz), 4.45 (1H, d, J=12 Hz), 4.49 (1H,  
35 d, J=12 Hz), 4.82 (1H, m), 5.14 (1x1/3H, m), 6.91 (1x1/3H, m), 6.91  
(1x1/3H, d, J=7 Hz), 6.95 (1x2/3H, d, J=7 Hz), 7.11-7.40 (10H, m),

7.49 (1x1/3H, d, J=10 Hz), 7.52 (1x2/3H, d, J=10 Hz), 8.50 (1x2/3H, d, J=8 Hz), 8.82 (1x1/3H, d, J=8 Hz);

MASS (ES-): m/e 777.

#### Preparation 63

5       Compound (63) was obtained in a manner similar to Preparation (17) except that 1N sodium hydroxide aqueous solution was used instead of the hydrogenation catalyst.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.52 (9x5/9H, s), 0.72 (9x4/9H, s), 1.10-1.90 (10H, m), 1.22 (3H, d, J=7 Hz), 1.35 (9x5/9H, s), 1.37 (9x4/9H, s), 2.15 (2H, m), 2.42-2.60 (2H, m), 2.70-3.00 (2H, m), 3.08-3.65 (2H, m), 3.95 (1H, m), 3.96 (1H, q, J=7 Hz), 4.10 (1x4/9H, dd, J=8, 4 Hz), 4.24 (1x5/9H, d, J=10 Hz), 4.27 (1x4/9H, d, J=10 Hz), 4.38 (1x4/9H, m), 4.45 (1H, d, J=12 Hz), 4.49 (1H, d, J=12 Hz), 4.83 (1x5/9H, m), 5.02 (1x5/9H, m), 6.91 (1x5/9H, d, J=7.5 Hz), 6.95 (1x4/9H, d, J=7.5 Hz), 7.10-7.40 (10H, m), 7.48 (1x5/9H, brd, J=10 Hz), 7.51 (1x4/9H, brd, J=19 Hz), 8.41 (1x4/9H, d, J=8 Hz), 8.79 (1x5/9H, d, J=8 Hz);

MASS (ES-): m/e 763.

#### Preparation 64

20       Compound (64) was obtained in a manner similar to Preparation (18). The obtained compound was used in Preparation 108.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.52 (9x1/2H, s), 0.73 (9x1/2H, s), 1.10-1.50 (4H, m), 1.21 (3x1/2H, d, J=6.5 Hz), 1.22 (3x1/2H, d, J=6.5 Hz), 1.58-1.96 (6H, m), 2.12-2.29 (2H, m), 2.35-2.60 (2H, m), 2.70-3.00 (2H, m), 3.06-3.66 (2H, m), 3.95 (1H, m), 3.96 (1x1/2H, q, J=6.5 Hz), 3.97 (1x1/2H, q, J=6.5 Hz), 4.10 (1x1/2H, m), 4.26-4.54 (3+1/2H, m), 4.85 (1x1/2H, m), 5.06 (1x1/2H, m), 7.14-7.41 (10H, m), 8.09 (2H, br), 8.55 (1x1/2H, d, J=8.5 Hz), 8.60 (1x1/2H, d, J=9 Hz), 8.67 (1x1/2H, d, J=8 Hz), 8.88 (1x1/2H, d, J=7 Hz);

MASS (ES-): m/e 663.

#### 30   Preparation 65

2-Chlorotrityl chloride resin (Nova Biochem, 0.9 mmol Cl/gram, 2.0 g) was washed with dichloromethane (3 ml) for 5 minutes twice. The resin was suspended in dichloromethane (3 ml) and to the suspension were added N-(9-fluorenylmethoxycarbonyl)-(R)-proline (1.82 g) in dichloromethane (3 ml) and N,N-diisopropylethylamine (698 mg). The suspension was shaken using rotary shaker for 15 minutes.

Additionally, N,N-diisopropylethylamine (1.05 g) was added to the suspension and the mixture was shaken for 1 hour. The reagents and solvent were washed away and the residual solid was washed with dichloromethane (20 ml, 5 times), N,N-dimethylformamide (20 ml, 3 times), dichloromethane (20 ml, 3 times) and isopropyl alcohol (20 ml). The resulting solid was dried under vacuum to give Compound (65) (2.89 g).

To determine the loading value, the Compound (65) (300 mg) was treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 6 ml) for 1 hour. The Compound (65) was filtered and the filtrate was concentrated in vacuo to give 107 mg of N-(9-fluorenylmethoxycarbonyl)-(R)-proline (107 mg) which was identical with the starting material by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5 mm) (Kanto Chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 50:50 rt=12.15 minutes.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.78-2.34 (4H, m), 3.32-3.50 (2H, m), 4.11-4.37 (4H, m), 7.10-7.38 (3H, m), 7.43 (2H, t, J=7.7 Hz), 7.62-7.71 (2H, m), 7.90 (2H, dd, J=7.8, 4.1 Hz).

#### Preparation 66

A solution of piperidine in N,N-dimethylformamide (20% v/v, 20 ml) was added to the Compound B1-1 (2.00 g) and the resulting suspension was shaken using rotary shaker for 15 minutes. The suspension was filtered and then a solution of piperidine in N,N-dimethylformamide (20% v/v, 20 ml) was added to the residual solid. The suspension was shaken for additional 15 minutes. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (20 ml, 5 times). To the residual solid were added (S)-N-(9-fluorenylmethoxycarbonyl)phenylalanine (2.46 g), benzotriazole-1-yloxy-tris-pyrrolidinophosphonium hexafluorophosphate (PyBOP®; 3.31 g) and N,N-diisopropylethylamine (822 mg) at ambient temperature and the resulting suspension was shaken at the same temperature for 16 hours. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (20 ml, 5 times), dichloromethane (20 ml, 3 times) and isopropyl alcohol, and dried to give Compound (66) (2.08 g).

To determine the loading value, the Compound (66) (200 mg) was

treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 4 ml) for 1 hour. The Compound (66) was filtered and the filtrate was concentrated in vacuo to give a dipeptide compound (79 mg). The purity of the dipeptide compound was determined by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5 mm) (Kanto Chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 50:50 rt=20.64 minutes. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.50-1.71 (2H, m), 1.74-1.91 (1H, m), 2.16-2, 34 (1H, m), 3.00 (1H, dd, J=12.5, 9.6 Hz), 3.12 (1H, dd, J=12.5, 5.7 Hz), 3.49-3.62 (1H, m), 4.21 (1H, t, J=6.6 Hz), 4.38 (2H, d, J=6.6 Hz), 4.65-4.80 (1H, m), 5.71 (1H, d, J=9.2 Hz), 7.12-7.46 (9H, m), 7.59 (2H, t, J=7.0 Hz), 7.77 (2H, d, J=7.4 Hz); MASS (ES<sup>+</sup>): m/e 485.13 (M+1).

#### Preparation 67

A solution of piperidine in N,N-dimethylformamide (20% v/v, 20 ml) was added to the Compound (66) (1.6 g), and the resulting suspension was shaken using rotary shaker for 15 minutes. The suspension was filtered and then 20% N,N-dimethylformamide solution of piperidine (15 ml) was added to the residual solid and the suspension was shaken for additional 15 minutes. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (20 ml, 3 times). To the solid were added (S)-6-benzoyloxy-2-N-tert-butoxycarbonylamino hexanoic acid (1.53 g), benzotriazole-1-yloxy-tris-pyrrolidinephosphonium hexafluorophosphate (PyBOP®; 2.34 g) and N,N-diisopropylethylamine (581 mg) at ambient temperature and the resulting suspension was shaken at the same temperature for 16 hours. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (10 ml, twice), isopropyl alcohol (10 ml), dichloromethane (10 ml, twice). This washing cycle was repeated once and then the solid was washed with isopropyl alcohol (10 ml) and diethyl ether (10 ml) successively, and dried to give Compound (67) (1.80 g).

To determine the loading value, the Compound (67) (300 mg) was treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 4 ml) for 1 hour. The Compound (67) was filtered and the filtrate was concentrated in vacuo and the residual solvent was removed azeotropically with toluene to give a tripeptide compound.

The purity of the tripeptide compound was determined by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5 mm) (Kanto chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 40:60 rt=7.76 minutes.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.66-0.83 (3H, m), 1.19-2.38 (9H, m), 2.68-2.85 (1H, m), 2.91-3.12 (2H, m), 3.58-3.74 (1H, m), 4.11-4.25 (1H, m); 4.30-4.46 (3H, m), 4.98 (1H, brs), 5.71 (1H, brs), 7.11-7.52 (10H, m), 7.60 (2H, d, J=6.9 Hz), 7.76 (2H, d, J=7.3 Hz);  
MASS (ES+): m/e 584.39 (M+1).

#### Preparation 68

10        A solution of piperidine in N,N-dimethylformamide (20% v/v, 100 ml) was added to the Compound (67) (1.15 g) and the suspension was shaken using rotary shaker for 15 minutes. The suspension was filtered, then a solution of piperidine in N,N-dimethylformamide (20% v/v, 100 ml) was added to the residual solid, and the suspension was  
15        shaken for additional 15 minutes. The suspension was filtered and washed with N,N-dimethylformamide (15 ml, 5 times). To the residual solid were added Compound (5) (1.15 g), benzotriazole-1-yloxy-tris-pyrrolidinephosphonium hexafluorophosphate (PyBOP®; 1.69 g) and N,N-diisopropylethylamine (420 mg) at ambient temperature and the  
20        resulting suspension was shaken at the same temperature for 36 hours. The suspension was filtered and the residual solid was washed with N,N-dimethylformamide (10 ml, twice), isopropyl alcohol (10 ml), dichloromethane (10 ml, twice). This washing cycle was repeated and then the residual solid was washed with isopropyl alcohol (10 ml) and  
25        diethyl ether (20 ml) successively to give Compound (68) (300 mg).

#### Preparation 69

30        The Compound (68) (300 mg) was treated with a mixture of dichloromethane-trifluoroacetic acid (1:1 v/v, 6 ml) for 1 hour. The suspension was filtered and the filtrate was concentrated in vacuo to give Compound (69) (128 mg). The purity of the Compound B1-5 was determined by HPLC analysis. Mightysil RP-18 GP 250-4.6 (5 mm) (Kanto chemical Co., Ltd.), 0.1% TFA-acetonitrile/0.1% TFA-water 40:60 rt=7.76 minutes. The Compound (69) was used in Preparation 103.

35        <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.69 (3H, t, J=6.8 Hz), 1.28 (3H, s), 1.46-1.70 (3H, m), 1.71-2.08 (9H, m), 2.84-3.04 (3H, m), 3.63-3.78 (1H, m), 4.04-4.15 (1H, m), 4.20-4.38 (3H, m), 4.79-4.90 (1H, m), 7.11-7.32 (6H,

m), 7.41 (2H, t, J=8.1 Hz), 7.45-7.62 (2H, m), 7.73-8.14 (5H, m);  
MASS (ES+); m/e 595.21 (M+1).

#### Preparation 70

Compound (70) was obtained in a manner similar to Preparations  
5 68.

#### Preparation 71

Compound (71) was obtained in a manner similar to Preparation  
69. The obtained compound was used in Preparation 97.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.67 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.51-  
10 1.63 (2H, m), 1.63-2.06 (10H, m), 2.36 (3H, s), 2.83-3.0 (2H, m), 3.0-  
3.15 (1H, m), 3.68-3.78 (1H, m), 4.0-4.10 (1H, m), 4.26-4.40 (3H, m),  
4.84 (1H, m), 5.20-5.45 (1H, brs), 7.10-7.32 (4H, m), 7.41 (2H, t,  
J=7.6 Hz), 7.52 (1H, t, J=7.3 Hz), 7.66 (1H, brd, J=3.3 Hz), 7.80-8.10  
(1H, brs), 7.99 (2H, d, J=6.9 Hz).

#### 15 Preparation 72

Compound (72) was obtained in a manner similar to Preparation  
69. The obtained compound was used in Preparation 82.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.69 (3H, t, J=7.3 Hz), 1.32 (3H, s), 1.46-  
2.24 (12H, m), 2.81-3.11 (3H, m), 3.65-3.79 (1H, m), 3.97-4.58 (4H, m),  
20 4.82-4.95 (1H, m), 6.95 (2H, t, J=8.8 Hz), 7.11-7.31 (4H, m), 7.36-  
7.82 (4H, m), 7.99 (2H, d, J=7.0 Hz), 8.04 (1H, brs);  
MASS (ES+): m/e 613.21 (M+1, free).

#### Preparation 73

Compound (73) was obtained in a manner similar to Preparations  
25 68. The obtained compound was used in Preparation 109.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, t, J=7.4 Hz), 1.29 (3H, s), 1.44-  
2.11 (12H, m), 2.80-3.03 (3H, m), 3.63-3.78 (1H, m), 3.76 (3H, s),  
4.02-4.46 (4H, m), 4.75-4.88 (1H, m), 6.79 (2H, d, J=8.3 Hz), 7.09 (2H,  
d, J=8.3 Hz), 7.14-7.31 (2H, m), 7.36-7.80 (4H, m), 8.00 (2H, d, J=7.4  
30 Hz), 8.13 (1H, brs);  
MASS (ES+): m/e 625.28 (M+1, free).

#### Preparation 74

Compound (74) was obtained in a manner similar to Preparations  
68. The obtained compound was used in Preparation 106.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.58-0.94 (6H, m), 0.95-1.33 (2H, m), 1.49-  
2.16 (16H, m), 3.00 (2H, brd, J=8.1 Hz), 3.03-3.18 (1H, m), 3.68-3.87

(1H, m), 4.02-4.16 (1H, m), 4.19-4.38 (3H, m), 4.67-4.83 (1H, m), 4.73-5.16 (2H, m), 7.11-7.35 (5H, m), 7.36-7.84 (4H, m), 7.94-8.19 (1H, brs), 7.97-8.04 (2H, m);

MASS (ES+): m/e 637.23 (M+1, free).

5 Preparation 75

Compound (75) was obtained in a manner similar to Preparation 68. The obtained compound was used in Preparation 100.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.48 (3H, t, J=7.3 Hz), 0.64 (3H, t, J=7.2 Hz), 0.72-0.91 (2H, m), 1.52-2.17 (12H, m), 2.91-3.11 (3H, m), 3.70-3.83 (1H, m), 3.97-4.43 (4H, m), 4.74-5.03 (1H, m), 7.13-7.34 (5H, m), 7.37-7.72 (4H, m), 7.76-7.84 (1H, m), 7.95-8.18 (2H, m), 7.97-8.04 (2H, m).

Preparation 76

To a stirred solution of benzotriazol-1-yl-oxy-tris-(N,N-dimethylamino)phosphoniumhexafluorophosphate (23.9 g) and 4-(N,N-dimethylamino)pyridine (7.6 g) in dry N,N-dimethylformamide (1.5 L), the Compound (18) (4.64 g) in dry N,N-dimethylformamide (8 ml) was added dropwise over 20 hours at room temperature. The volatiles were removed under reduced pressure and the residue was diluted with ethyl acetate (300 ml). The precipitate formed was collected by filtration, dissolved in ethyl acetate (50 ml), then washed with 5% aqueous potassium hydrogen sulfate solution (100 ml, 4 times), saturated aqueous sodium bicarbonate solution (100 ml, 3 times), water (100 ml) and brine (100 ml). The organic layer was dried over anhydrous magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (eluting with ethyl acetate/hexane = 1:1 v/v) to give Compound (76) (3.083 g) as a colorless amorphous.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.0 Hz), 1.28 (3H, s), 1.36-1.55 (2H, m), 1.59-1.99 (4H, m), 2.04-2.24 (2H, m), 2.24-2.40 (2H, m), 2.90 (1H, dd, J=13.6, 6.6 Hz), 3.19 (1H, dd, J=13.6, 9.9 Hz), 3.20-3.31 (1H, m), 3.80-3.91 (1H, m), 4.18-4.28 (1H, m), 4.32 (2H, t, J=6.2 Hz), 4.67 (1H, brd, J=5.5 Hz), 5.03 (2H, s), 5.14 (1H, dt, J=10 and 5.6 Hz), 5.85 (1H, s), 6.89 (2H, d, J=8.6 Hz), 7.14 (1H, s), 7.15 (2H, d, J=8.6 Hz), 7.28-7.48 (9H, m), 7.49-7.60 (2H, m), 8.00-8.06 (2H, m);

MASS (ES+): m/e 683.49 (M+1).

Preparation 77

To a stirred solution of the Compound (76) (3.07 g) in methanol (30 ml) was added 1N aqueous sodium hydroxide solution (11.2 ml, 2.5 eq) under ice-cooling and the mixture was stirred at ambient  
5 temperature for 4 hours. The pH of the mixture was adjusted to pH 7 with 1N hydrogen chloride, then methanol was evaporated under reduced pressure. The residue was extracted with ethyl acetate (300 ml). The organic layer was washed with saturated aqueous ammonium chloride (50 ml, twice), water (50 ml) and brine (50 ml), dried over sodium sulfate  
10 and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (ethyl acetate, then methanol/ethyl acetate = 5:95 v/v) to give Compound (77) (2.63 g) as a colorless amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.4 Hz), 1.28 (3H, s), 1.20-  
15 1.92 (8H, m), 2.07-2.23 (2H, m), 2.24-2.39 (2H, m), 2.89 (1H, dd, J=13.8, 6.1 Hz), 3.18 (1H, dd, J=13.8, 9.5 Hz), 3.15-3.28 (1H, m), 3.65 (2H, d, J=6.5 Hz), 3.78-3.91 (1H, m), 4.15-4.28 (1H, m), 4.67 (1H, brd, J=5.8 Hz), 5.03 (2H, s), 5.13 (1H, dt, J=9.5, 6.2 Hz), 5.93 (1H, s), 6.88 (2H, d, J=8.5 Hz), 7.11-7.15 (1H, m), 7.14 (2H, d, J=8.5 Hz),  
20 7.27-7.45 (5H, m), 7.52 (1H, d, J=10.2 Hz);  
MASS (ES+): m/e 579.30 (M+1).

Preparation 78

To a stirred solution of the Compound (77) (1.0 g) in dichloromethane (50 ml) was added 1,1,1-triacetoxy-1,1-dihydro-1,2-  
25 benziiodoxol-3(1H)-one (Dess-Martin periodinane) (3.66 g) in one portion under ice-cooling. The mixture was stirred at ambient temperature for 2 hours. The reaction was quenched with a solution of 20% sodium thiosulfate in saturated aqueous sodium bicarbonate solution (100 ml) under ice-cooling, then the mixture was extracted  
30 with ethyl acetate (100 ml), washed with saturated aqueous sodium bicarbonate solution, water and brine, dried over sodium sulfate, and evaporated in vacuo to give Compound (78) as a colorless amorphous (980 mg). The obtained compound was used in Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.30 (3H, s), 1.50-  
35 1.91 (6H, m), 2.08-2.38 (4H, m), 2.46-2.55 (2H, brt, J=6.8 Hz), 2.90 (1H, dd, J=13.7, 5.9 Hz), 3.18 (1H, dd, J=13.7, 7.3 Hz), 3.20-3.30 (1H,

m), 3.80-3.91 (1H, m), 4.17-4.29 (1H, m), 4.68 (1H, brd, J=6.3 Hz), 5.03 (2H, s), 5.14 (1H, dt, J=9.5, 5.6 Hz), 5.90 (1H, s), 6.89 (2H, d, J=8.5 Hz), 7.10-7.21 (1H, m), 7.14 (2H, d, J=8.5 Hz), 7.22-7.45 (5H, m), 7.47 (1H, d, J=10.3 Hz), 9.77 (1H, s);

5 MASS (ES+): m/e 577.25 (M+1).

#### Preparation 79

Compound (79) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.46  
10 (2H, m), 1.60-1.98 (6H, m), 2.06-2.40 (4H, m), 2.90 (1H, dd, J=14, 6 Hz), 3.18 (1H, dd, J=14, 10 Hz), 3.26 (1H, m), 3.77 (3H, s), 3.86 (1H, m), 4.24 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.67 (1H, m), 5.14 (1H, ddd, J=10, 10, 6 Hz), 5.85 (1H, s), 6.81 (2x1H, d, J=9 Hz), 7.14 (2x1H, d, J=9 Hz), 7.14 (1H, d, J=10 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.50-  
15 7.60 (2H, m), 8.03 (2x1H, d, J=7.5 Hz);

MASS (ES-): m/e 605.

#### Preparation 80

Compound (80) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.25-1.51 (2H, m),  
20 1.28 (3H, s), 1.54-1.94 (6H, m), 2.08-2.40 (4H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.25 (1H, m), 3.65 (2H, m), 3.77 (3H, s), 3.85 (1H, m), 4.22 (1H, dt, J=10 and 7.5 Hz), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.99 (1H, s), 6.81 (2x1H, d, J=8.7 Hz), 7.14 (2x1H, d, J=8.7 Hz), 7.15 (1H, d, J=10 Hz), 7.53 (1H, d, J=10 Hz);

MASS (ES-): m/e 501.

#### Preparation 81

Compound (81) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 2.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.53-1.90 (6H, m), 2.08-2.37 (4H, m), 2.50 (2H, m), 2.89 (1H, dd, J=14, 6 Hz), 3.17 (1H, dd, J=14, 10 Hz), 3.25 (1H, m), 3.86 (1H, m), 4.23 (1H, m), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.89 (1H, s), 6.81  
35 (2x1H, d, J=8.8 Hz), 7.14 (2x1H, d, J=8.8 Hz), 7.16 (1H, d, J=11 Hz), 7.48 (1H, d, J=10 Hz), 9.77 (1H, t, J=1.4 Hz);

MASS (ES-): m/e 499.

Preparation 82

Compound (82) was obtained in a manner similar to Preparation 76.

5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.35-  
1.98 (8H, m), 2.06-2.40 (4H, m), 2.93 (1H, dd, J=13.6, 6.8 Hz), 3.20  
(1H, dd, J=13.6, 9.6 Hz), 3.21-3.33 (1H, m), 3.78-3.90 (1H, m), 4.18-  
4.30 (1H, m), 4.32 (2H, t, J=6.4 Hz), 4.68 (1H, brd, J=7.7 Hz), 5.07-  
5.20 (1H, m), 5.84 (1H, s), 6.96 (2H, t, J=8.6 Hz), 7.10 (1H, d,  
10 J=10.3 Hz), 7.19 (1H, dd, J=8.6, 5.5 Hz), 7.44 (2H, t, J=7.3 Hz),  
7.52-7.61 (2H, m), 8.03 (2H, d, J=8.4 Hz);

MASS (ES+): m/e 595.39 (M+1).

Preparation 83

15 Compound (83) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.23-1.95 (8H, m),  
1.29 (3H, s), 2.08-2.41 (4H, m), 2.94 (1H, dd, J=13.6, 6.2 Hz), 3.21  
(1H, dd, J=13.6, 9.6 Hz), 3.23-3.33 (1H, m), 3.67 (2H, brt, J=6.2 Hz),  
3.80-3.91 (1H, m), 4.16-4.30 (1H, m), 4.69 (1H brd, J=5.5 Hz), 5.07-  
20 5.20 (1H, m), 5.97 (1H, s), 6.97 (2H, t, J=8.5 Hz), 7.11 (1H, d,  
J=10.2 Hz), 7.20 (2H, dd, J=8.5, 5.1 Hz), 7.57 (1H, d, J=10.2 Hz);

MASS (ES+): m/e 491.45 (M+1).

Preparation 84

25 Compound (84) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=6.9 Hz), 1.29 (3H, s), 1.53-  
1.90 (6H, m), 2.08-2.38 (4H, m), 2.50 (2H, brt, J=7.0 Hz), 2.93 (1H,  
dd, J=13.9, 6.2 Hz), 3.19 (1H, dd, J=13.9, 9.1 Hz), 3.20-3.31 (1H, m),  
3.79-3.90 (1H, m), 4.17-4.28 (1H, m), 4.68 (1H, brd, J=6.0 Hz), 5.07-  
30 5.19 (1H, m), 5.87 (1H, s), 6.96 (2H, t, J=8.9 Hz), 7.10 (1H, d,  
J=10.1 Hz), 7.19 (2H, dd, J=8.9, 5.5 Hz), 7.50 (1H, d, J=10.3 Hz),  
9.77 (1H, s);

MASS (ES+): m/e 489.42 (M+1).

Preparation 85

35 Compound (85) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.31-1.96 (14H, m), 2.08-2.23 (1H, m),  
2.24-2.37 (2H, m), 2.43-2.56 (2H, m), 2.95 (1H, dd, J=13.5, 5.7 Hz),  
3.14-3.28 (1H, m), 3.26 (1H, dd, J=13.5, 10.5 Hz), 3.84-3.95 (1H, m),  
4.23 (1H, dt, J=10.2, 7.8 Hz), 4.31 (2H, t, J=6.6 Hz), 4.63-4.69 (1H,  
5 m), 5.15 (1H, ddd, J=10.2, 10.2, 6.0 Hz), 6.13 (1H, s), 7.16-7.31 (6H,  
m), 7.39-7.48 (3H, m), 7.52-7.60 (1H, m), 8.00-8.05 (2H, m);

MASS (ES+): m/e 589.40 (M+1).

#### Preparation 86

Compound (86) was obtained in a manner similar to Preparation  
10 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.20-1.81 (14H, m), 2.10-2.22 (1H, m),  
2.25-2.37 (2H, m), 2.43-2.58 (2H, m), 2.95 (1H, dd, J=13.5, 5.7 Hz),  
3.13-3.28 (1H, m), 3.25 (1H, dd, J=13.5, 10.2 Hz), 3.65 (2H, t, J=6.3  
Hz), 3.85-3.95 (1H, m), 4.22 (1H, dt, J=10.2, 7.2 Hz), 4.67 (1H, dd,  
15 J=7.8, 2.1 Hz), 5.15 (1H, ddd, J=10.2, 10.2, 6.0 Hz), 6.28 (1H, s),  
7.16-7.31 (6H, m), 7.44 (1H, d, J=10.2 Hz);

MASS (ES+): m/e 485.39 (M+1).

#### Preparation 87

Compound (87) was obtained in a manner similar to Preparation ..  
20 78. The obtained compound was used in Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.42-1.92 (13H, m), 2.08-2.22 (1H, m),  
2.23-2.37 (2H, m), 2.42-2.56 (2H, m), 2.95 (1H, dd, J=13.8, 5.7 Hz),  
3.13-3.28 (1H, m), 3.25 (1H, dd, J=13.8, 10.2 Hz), 3.85-3.95 (1H, m),  
4.22 (1H, dt, J=10.2, 7.2 Hz), 4.64-4.69 (1H, m), 5.15 (1H, ddd, J=9.9,  
25 9.9, 5.7 Hz), 6.15 (1H, s), 7.17-7.31 (6H, m), 7.44 (1H, d, J=10.2 Hz),  
9.77 (1H, s);

MASS (ES+): m/e 483.36 (M+1).

#### Preparation 88

Compound (88) was obtained in a manner similar to Preparation  
30 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.790 (3H, t, J=7.2 Hz), 1.27 (3H, s),  
1.38-1.98 (8H, m), 2.07-2.38 (4H, m), 3.06 (1H, dd, J=14.1, 6.9 Hz),  
3.28-3.36 (1H, m), 3.26 (1H, dd, J=14.1, 8.4 Hz), 3.79-3.89 (1H, m),  
4.25 (1H, dt, J=10.2, 7.8 Hz), 4.32 (2H, t, J=6.3 Hz), 4.65-4.71 (1H,  
35 m), 5.17 (1H, dt, J=9.0, 6.9 Hz), 5.89 (1H, s), 7.01 (1H, d, J=10.2  
Hz), 7.32-7.38 (2H, m), 7.40-7.48 (2H, m), 7.52-7.63 (3H, m), 7.61-

7.67 (1H, m), 8.00-8.06 (2H, m);

MASS (ES+): m/e 602.47 (M+1).

Preparation 89

Compound (89) was obtained in a manner similar to Preparation  
5 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.809 (3H, t, J=7.2 Hz), 1.24-1.94 (9H, m),  
1.28 (3H, s), 2.06-2.41 (4H, m), 3.06 (1H, dd, J=9.0, 6.9 Hz), 3.26-  
3.36 (1H, m), 3.26 (1H, dd, J=13.5, 9.0 Hz), 3.66 (2H, t, J=6.3 Hz),  
3.79-3.90 (1H, m), 4.24 (1H, dt, J=10.2, 7.8 Hz), 4.65-4.72 (1H, m),  
10 5.18 (1H, dt, J=9.0, 7.2 Hz), 6.01 (1H, s), 7.02 (1H, d, J=10.2 Hz),  
7.35 (2H, d, J=8.1 Hz), 7.58 (2H, d, J=8.1 Hz), 7.64 (1H, d, J=10.2  
Hz);

MASS (ES+): m/e 498.41 (M+1).

Preparation 90

15 Compound (90) was obtained in a manner similar to Preparation  
78. The obtained compound was used in Example 5.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.812 (3H, t, J=7.2 Hz), 1.29 (3H, s),  
1.49-1.92 (6H, m), 2.07-2.40 (4H, m), 2.51 (2H, t, J=7.2 Hz), 3.06 (1H,  
dd, J=13.5, 6.9 Hz), 3.26-3.36 (1H, m), 3.26 (1H, dd, J=13.5, 8.7 Hz),  
20 3.78-3.90 (1H, m), 4.24 (1H, dt, J=10.2, 7.2 Hz), 4.65-4.71 (1H, m),  
5.18 (1H, dt, J=9.0, 8.4 Hz), 5.93 (1H, s), 7.02 (1H, d, J=10.2 Hz),  
7.35 (2H, d, J=8.7 Hz), 7.57-7.59 (1H, m), 7.58 (2H, d, J=8.8 Hz),  
9.77 (1H, s);

MASS (ES+): m/e 496.46 (M+1).

25 Preparation 91

Compound (91) was obtained in a manner similar to Preparation  
76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.5 Hz), 1.27 (3H, s), 1.39.  
(3H, t, J=7.2 Hz), 1.40-1.52 (2H, m), 1.64-1.98 (6H, m), 2.06-2.39 (4H,  
30 m), 2.88 (1H, dd, J=13.5, 5.7 Hz), 3.09-3.32 (2H, m), 3.79-3.90 (1H,  
m), 3.99 (2H, q, J=7.2 Hz), 4.18-4.30 (1H, m), 4.31 (2H, t, J=6.0 Hz),  
4.62-4.69 (1H, m), 5.07-5.18 (1H, dt, J=9.9, 6.0 Hz), 5.82 (1H, s),  
6.79 (2H, d, J=8.4 Hz), 7.10-7.18 (1H, m), 7.13 (2H, d, J=8.4 Hz),  
7.38-7.59 (4H, m), 7.99-8.05 (2H, m);

35 MASS (ES+): m/e 621.55 (M+1).

Preparation 92

Compound (92) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.2 Hz), 1.28-1.93 (8H, m), 1.28 (3H, s), 1.39 (3H, t, J=6.9 Hz), 2.08-2.23 (2H, m), 2.24-2.39 (2H, m), 2.88 (1H, dd, J=13.5, 6.0 Hz), 3.17 (1H, dd, J=13.5, 9.9 Hz), 3.20-3.30 (1H, m), 3.65 (2H, t, J=6.6 Hz), 3.80-3.90 (1H, m), 3.99 (2H, q, J=6.9 Hz), 4.22 (1H, dt, J=10.2, 7.8 Hz), 4.64-4.69 (1H, m), 5.13 (1H, dt, J=9.9, 6.0 Hz), 5.93 (1H, s), 6.79 (2H, d, J=8.4 Hz), 7.10-7.17 (1H, m), 7.13 (2H, d, J=8.4 Hz), 7.52 (1H, d, J=10.2 Hz);  
MASS (ES+): m/e 517.44 (M+1).

#### Preparation 93

Compound (93) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.2 Hz), 1.29 (3H, s), 1.40 (3H, t, J=6.9 Hz), 1.49-1.92 (6H, m), 2.09-2.24 (2H, m), 2.24-2.39 (2H, m), 2.50 (2H, dt, J=6.3, 1.2 Hz), 2.88 (1H, dd, J=14.1, 5.7 Hz), 3.17 (1H, dd, J=14.1, 10.2 Hz), 3.20-3.30 (1H, m), 3.81-3.90 (1H, m), 3.99 (2H, q, J=6.9 Hz), 4.23 (1H, dt, J=10.2, 7.2 Hz), 4.64-4.70 (1H, m), 5.13 (1H, dt, J=10.2, 5.7 Hz), 5.85 (1H, s), 6.80 (2H, d, J=8.4 Hz), 7.12-7.19 (1H, m), 7.13 (2H, d, J=8.4 Hz), 7.46 (1H, d, J=10.2 Hz), 9.77 (1H, t, J=1.2 Hz);  
MASS (ES+): m/e 515.36 (M+1).

#### Preparation 94

Compound (94) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.5 Hz), 1.25 (3H, s), 1.46 (2H, m), 1.58-1.95 (6H, m), 2.07-2.39 (4H, m), 3.11 (1H, dd, J=14, 8 Hz), 3.16 (1H, dd, J=14, 8 Hz), 3.41 (1H, m), 3.88 (1H, m), 4.24 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.70 (1H, dd, J=8, 3 Hz), 5.24 (1H, ddd, J=10, 8, 8 Hz), 5.80 (1H, s), 6.97-7.31 (5H, m), 7.44 (2H, dd, J=7.5, 7.5 Hz), 7.50-7.60 (2H, m), 8.00-8.06 (2H, m);  
MASS (ES+): m/e 595;  
MASS (ES-): m/e 593.

#### Preparation 95

Compound (95) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7.5 Hz), 1.22-1.51 (2H, m), 1.26 (3H, s), 1.52-1.73 (3H, m), 1.74-1.94 (3H, m), 2.08-2.40 (4H, m), 3.10 (1H, dd, J=15, 8 Hz), 3.15 (1H, dd, J=15, 8 Hz), 3.41 (1H, m), 3.66 (2H, t, J=7 Hz), 3.88 (1H, m), 4.23 (1H, m), 4.70 (1H, m), 5.24 (1H, ddd, J=10, 8, 8 Hz), 5.91 (1H, s), 6.97-7.08 (2H, m), 7.10 (1H, d, J=10 Hz), 7.15-7.28 (2H, m), 7.54 (1H, d, J=10 Hz);

MASS (ES+): m/e 491;

MASS (ES-): m/e 489.

#### Preparation 96

10 Compound (96) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 7.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7 Hz), 1.26 (3H, s), 1.50-1.94 (6H, m), 2.11-2.44 (4H, m), 2.51 (2H, m), 3.05-3.20 (2H, m), 3.41 (1H, m), 3.89 (1H, m), 4.24 (1H, m), 4.71 (1H, m), 5.24 (1H, m), 5.85 (1H, s), 6.97-7.28 (5H, m), 7.49 (1H, d, J=10 Hz), 9.78 (1H, s);

MASS (ES+): m/e 489;

MASS (ES-): m/e 487.

#### Preparation 97

20 Compound (97) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.25-1.47 (2H, m), 1.56-1.74 (4H, m), 1.76-1.89 (2H, m), 2.15-2.36 (4H, m), 2.93 (1H, dd, J=13.6, 6.6 Hz), 3.20 (1H, dd, J=13.6, 9.5 Hz), 3.20-3.32 (1H, m), 3.66 (2H, t, J=6.6 Hz), 3.85 (1H, ddd, J=13.2, 8.1, 4.4 Hz), 4.22 (1H, ddd, J=15, 7.6, 2.2 Hz), 4.67 (1H, brd, J=5.8 Hz), 5.15 (1H, ddd, J=16.5, 9.5, 6.6 Hz), 5.99 (1H, s), 7.08 (1H, d, J=10.6 Hz), 7.16 (2H, d, J=8.9 Hz), 7.22 (2H, d, J=8.9 Hz), 7.58 (1H, d, J=10.3 Hz).

#### Preparation 98

30 Compound (98) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.41-1.58 (2H, m), 1.61 (3H, s), 1.71-1.90 (4H, m), 2.05-2.34 (4H, m), 2.95 (1H, dd, J=13.5, 6.2 Hz), 3.20 (1H, dd, J=13.5, 9.2 Hz), 3.25-3.36 (1H, m), 3.82-3.89 (1H, m), 4.25 (1H, dd, J=17.9, 10.2 Hz), 4.32 (2H, t, J=6.2 Hz), 4.68 (1H, brd, J=6.6 Hz), 5.14 (1H, ddd, J=16.7, 9.5, 6.6

Hz), 5.81 (1H, s), 7.08 (1H, d, J=9.9 Hz), 7.16 (2H, d, J=8.1 Hz), 7.24 (2H, d, J=8.1 Hz), 7.44 (2H, t, J=8.4 Hz), 7.56 (1H, dd, J=6.6, 4.3 Hz), 8.03 (2H, d, J=7.3 Hz).

Preparation 99

5 Compound (99) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 8.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.5 Hz), 1.29 (3H, s), 1.52-1.90 (6H, m), 2.08-2.38 (4H, m), 2.50 (2H, m), 2.94 (1H, dd, J=13.5, 6 Hz), 3.19 (1H, dd, J=13.5, 9.5 Hz), 3.28 (1H, m), 3.85 (1H, m), 4.24 (1H, m), 4.68 (1H, m), 5.14 (1H, ddd, J=10, 9.5, 6 Hz), 5.89 (1H, s), 7.09 (1H, d, J=10.5 Hz), 7.16 (2x1H, d, J=8.5 Hz), 7.25 (2x1H, d, J=8.5 Hz), 7.52 (1H, d, J=10 Hz), 9.77 (1H, t, J=1.3 Hz);

MASS (ES-): m/e 503.

Preparation 100

15 Compound (100) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.75 (3H, t, J=7.3 Hz), 0.91 (3H, t, J=7.3 Hz), 1.35-1.98 (10H, m), 2.10-2.43 (4H, m), 2.97 (1H, dd, J=13.5, 6.4 Hz), 3.24 (1H, dd, J=13.5, 9.4 Hz), 3.21-3.30 (1H, m), 3.83-3.94 (1H, m), 4.25 (1H, dt, J=10.3, 7.6 Hz), 4.32 (2H, t, J=6.2 Hz), 4.63-4.70 (1H, m), 5.18 (1H, dt, J=10.2, 6.3 Hz), 5.78 (1H, s), 7.13 (1H, d, J=10.3 Hz), 7.19-7.32 (5H, m), 7.40-7.47 (2H, m), 7.50 (1H, d, J=10.2 Hz), 7.51-7.60 (1H, m), 8.01-8.06 (2H, m);

MASS (ES+): m/e 591.21 (M+1).

25 Preparation 101

Compound (101) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.7 Hz), 0.91 (3H, t, J=7.3 Hz), 1.20-1.93 (10H, m), 2.07-2.45 (4H, m), 2.97 (1H, dd, J=13.5, 6.2 Hz), 3.24 (1H, dd, J=13.5, 9.1 Hz), 3.21-3.30 (1H, m), 3.66 (2H, t, J=6.6 Hz), 3.82-3.93 (1H, m), 4.24 (1H, dd, J=10.0, 7.2 Hz), 4.67 (1H, brd, J=8.0 Hz), 5.12-5.23 (1H, m), 5.84 (1H, s), 7.12 (1H, d, J=10.0 Hz), 7.16-7.31 (5H, m), 7.49 (1H, d, J=10.4 Hz);

MASS (ES+): m/e 487.19 (M+1).

35 Preparation 102

Compound (102) was obtained in a manner similar to preparation

78. The obtained compound was used in Example 9.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.4 Hz), 0.91 (3H, t, J=7.4 Hz), 1.50-1.92 (8H, m), 2.07-2.42 (4H, m), 2.51 (2H, brt, J=6.1 Hz), 2.96 (1H, dd, J=13.1 and 5.7 Hz), 3.17-3.30 (2H, m), 3.83-3.94 (1H, m),  
5 4.18-4.30 (1H, m), 4.67 (1H, brd, J=6.1 Hz), 5.12-5.23 (1H, m), 5.85 (1H, s), 7.15 (1H, d, J=10.8 Hz), 7.18-7.31 (5H, m), 7.44 (1H, d, J=10.0 Hz), 9.77 (1H, s);  
MASS (ES+): m/e 485.29 (M+1).

#### Preparation 103

10 Compound (103) was obtained in a manner similar to Preparation 76 except that benzotriazol-1-yloxy-tris-pyrrolidinephosphonium hexafluorophosphate was used instead of benzotriazol-1-yloxy-tris-(dimethylamino)phosphonium hexafluorophosphate.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.46  
15 (2H, m), 1.61-2.00 (6H, m), 2.06-2.39 (4H, m), 2.97 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.24 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.67 (1H, m), 5.18 (1H, m), 5.82 (1H, s), 7.13 (1H, d, J=11 Hz), 7.16-7.32 (5H, m), 7.39-7.59 (2H, m), 7.51-7.60 (2H, m), 7.95-8.08 (2H, m);

20 MASS (ES-): m/e 575.

#### Preparation 104

Compound (104) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.5 Hz), 1.22-1.95 (8H, m),  
25 1.28 (3H, s), 2.07-2.40 (4H, m), 2.96 (1H, dd, J=13, 6.5 Hz), 3.04 (1H, dd, J=13, 9 Hz), 3.06 (1H, m), 3.65 (2H, brt, J=6 Hz), 3.86 (1H, m), 4.23 (1H, m), 4.68 (1H, m), 5.19 (1H, ddd, J=10, 9, 6 Hz), 5.93 (1H, s), 7.12 (1H, d, J=11 Hz), 7.16-7.32 (5H, m), 7.55 (1H, d, J=10 Hz);  
MASS (ES-): m/e 471.

#### Preparation 105

Compound (105) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 10.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.48-1.95 (6H, m), 2.06-2.59 (6H, m), 2.97 (1H, dd, J=13.5, 6 Hz), 3.24 (1H,  
35 dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.24 (1H, m), 4.68 (1H, dd, J=8, 2 Hz), 5.19 (1H, ddd, J=10, 10, 6 Hz), 5.92 (1H, s), 7.16 (1H,

d, J=11 Hz), 7.16-7.33 (5H, m), 7.50 (1H, d, J=10 Hz), 9.77 (1H, brs);  
MASS (ES-): m/e 469.

Preparation 106

Compound (106) was obtained in a manner similar to Preparation  
5 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.2 Hz), 0.96 (3H, t, J=7.0 Hz), 0.93-1.04 (1H, m), 1.11-1.36 (3H, m), 1.37-1.64 (3H, m), 1.65-1.96 (7H, m), 2.00-2.24 (2H, m), 2.27-2.42 (2H, m), 2.98 (1H, dd, J=13.6, 6.6 Hz), 3.21-3.32 (1H, m), 3.23 (1H, dd, J=13.6, 9.5 Hz),  
10 3.81-3.93 (1H, m), 4.18-4.29 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.67 (1H, brd, J=7.7 Hz), 5.10-5.23 (1H, m), 5.78 (1H, s), 7.13 (1H, d, J=10.2 Hz), 7.19-7.32 (5H, m), 7.40-7.60 (4H, m), 8.01-8.06 (2H, m);  
MASS (ES+): m/e 619.34 (M+1).

Preparation 107

15 Compound (107) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.89 (3H, t, J=7.0 Hz), 0.96 (3H, t, J=6.8 Hz), 0.97-1.08 (1H, m), 1.12-1.92 (13H, m), 2.02-2.26 (2H, m), 2.27-2.44 (2H, m), 2.98 (1H, dd, J=13.5, 6.6 Hz), 3.20-3.31 (1H, m), 3.22  
20 (1H, dd, J=13.5, 9.6 Hz), 3.66 (2H, brt, J=6.3 Hz), 3.82-3.92 (1H, m), 4.22 (1H, dt, J=10.2, 7.6 Hz), 4.67 (1H, brd, J=7.5 Hz), 5.11-5.22 (1H, m), 5.86 (1H, s), 7.12 (1H, d, J=10.3 Hz), 7.17-7.31 (5H, m), 7.49 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 515.23 (M+1).

25 Preparation 108

Compound (108) was obtained in a manner similar to Preparation  
78.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.89 (3H, t, J=6.6 Hz), 0.94-1.08 (1H, m),  
0.96 (3H, t, J=6.9 Hz), 1.10-1.38 (4H, m), 1.43-1.92 (6H, m), 2.00-  
30 2.42 (5H, m), 2.50 (2H, brt, J=6.6 Hz), 2.98 (1H, dd J=13.5, 6.6 Hz),  
3.20-3.31 (1H, m), 3.22 (1H, dd, J=13.5, 9.2 Hz), 3.81-3.92 (1H, m),  
4.16-4.28 (1H, m), 4.67 (1H, J=5.8 Hz), 5.10-5.22 (1H, m), 5.84 (1H, s),  
7.14 (1H, d, J=10.3 Hz), 7.15-7.32 (5H, m), 7.43 (1H, d, J=10.2 Hz), 9.77 (1H, brs);  
35 MASS (ES+): m/e 513.26 (M+1).

Preparation 109

Compound (109) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.04 (3x3H, s), 1.26-1.40 (4H, m), 1.33 (3H, d, J=7 Hz), 1.48-1.92 (6H, m), 2.16 (1H, m), 2.34 (1H, m), 2.54 (2H, m), 2.90 (1H, dd, J=13, 5 Hz), 3.02 (1H, m), 3.18 (1H, dd, J=13, 10 Hz), 3.90 (1H, m), 3.92 (1H, q, J=7 Hz), 4.32 (1H, dt, J=10, 7.5 Hz), 4.49 (1H, d, J=12 Hz), 4.55 (1H, d, J=12 Hz), 4.59 (1H, m), 5.01 (1H, ddd, J=10, 10, 5 Hz), 6.21 (1H, d, J=10 Hz), 6.23 (1H, d, J=10 Hz), 7.13 (1H, d, J=10 Hz), 7.16-7.41 (10H, m);

MASS (ES<sup>+</sup>): m/e 647.

Preparation 110

To a stirred solution of 2-indanone (12.5 g) in a mixture of ethanol (210 ml) and water (210 ml) was added sodium cyanide (11.6 g) and ammonium carbonate (100 g) at ambient temperature. The mixture was heated at 55 to 60°C for 6 hours and then allowed to cool to ambient temperature. The mixture was stirred at 0°C for half an hour and the precipitated solid was collected. The solid was recrystallized from ethanol to give 2-spirohydantoinindane (4.5 g).

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 3.04 (1H, s), 3.10 (1H, s), 3.22-3.42 (1H, br), 3.33 (1H, s), 3.38 (1H, s), 7.15-7.27 (4H, m), 10.25 (1H, brs);  
MASS (ES<sup>+</sup>): m/e 202.18 (M).

Preparation 111

To a stirred solution of 2-spirohydantoinindane in propylene glycol (13 ml) was added 40% aqueous solution of sodium hydroxide (22 ml) at ambient temperature. The mixture was refluxed for 24 hours. The reaction mixture was allowed to cool and then diluted with water (50 ml). After acidification with 1 N hydrochloric acid to pH 2, the precipitated solid was filtered and the filtrate was neutralized by addition of a 10% (w/v) aqueous sodium bicarbonate solution. The mixture was stirred for an hour and left overnight at 0°C. Most of the solvent was removed under reduced pressure and the residue was stirred at 0°C. The precipitate were collected by filtration and recrystallized from ethanol/water to give 2-aminoindan-2-carboxylic acid (2.76 g) as a white-scaled crystal.

<sup>1</sup>H-NMR (300 MHz, D<sub>2</sub>O, δ): 3.23 (1H, s), 3.29 (1H, s), 3.64 (1H, s),

3.70 (1H, s), 7.28-7.38 (4H, m);

MASS (ES+): m/e 178.00 (M+1).

#### Preparation 112

To a stirred solution of methyl (2R)-2-hydroxypropanoate (25 g) in N,N-dimethylformamide (250 ml) was added imidazole (66 g) followed by tert-butyldiphenylchlorosilane (68.08 g) at 0°C. The mixture was stirred at ambient temperature for two hours. The reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was successively washed with water, 0.2 N hydrochloric acid, saturated aqueous sodium bicarbonate solution and brine. The organic layer was dried over magnesium sulfate, filtered and evaporated to give methyl (2R)-2-tert-butyldiphenylsilylpropanoate (80.5 g) as a colorless oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (9H, s), 1.37 (3H, d, J=6.9 Hz), 3.56 (3H, s), 4.27 (1H, q, J=6.9 Hz), 7.32-7.48 (6H, m), 7.63-7.75 (4H, m); MASS (ES+): m/e 375.29 (M+Na).

#### Preparation 113

To a stirred solution of dimethyl methylphosphonate (145 g) in tetrahydrofuran (750 ml) was added n-butyllithium (1.6 M in hexane, 127 ml) dropwise at -78°C over an hour and the resulting mixture was stirred at the same temperature for an hour. To this mixture was added dropwise a solution of methyl-(2R)-2-tert-butyldiphenylsilyloxypropanoate in tetrahydrofuran (450 ml) over an hour. The mixture was stirred at the same temperature for two hours, allowed to warm to -30°C over an hour and stirred at ambient temperature for half an hour. The reaction mixture was poured into a stirred saturated ammonium chloride (2000 ml) in an ice bath and left at ambient temperature overnight. The aqueous phase was separated and extracted with ethyl acetate twice. The combined organic extracts were washed with water and brine, and dried over magnesium sulfate. The organic layer was filtered and concentrated in vacuo. The crude product was purified by flash chromatography eluting with 33 to 60% ethyl acetate/hexane (v/v) to give dimethyl-(3R)-3-tert-butyldiphenylsilyloxy-2-oxobutylphosphate (81.1 g) as a colorless oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 2.21 (3H, d, J=6.9 Hz), 3.08 (1H, dd, J=21.9, 15.0 Hz), 3.48 (1H, dd, J=20.4, 15.0 Hz), 3.73 (3H,

s), 3.77 (3H, s), 4.25 (3H, q, J=6.9 Hz), 7.33-7.49 (6H, m), 7.58-7.68 (4H, m);

MASS (ES+): m/e 435.31 (M+1).

#### Preparation 114

5 To a stirred solution of crude (2R)-2-aminobutanoic acid (12.1 g) in aqueous sulfuric acid (0.88 M, 200 ml) was added an aqueous sodium nitrite (8.8 M, 20 ml) dropwise at 0°C over two hours. The mixture was left at the same temperature and allowed to warm to ambient temperature. Additional concentrated sulfuric acid (10 ml) and aqueous sodium nitrite (12.1 g) were added at 0°C after thirteen hours and the mixture was left at ambient temperature for two days. Half of the volume of the solvent was evaporated under reduced pressure and the resulting solution was adjusted to pH 2 with saturated aqueous sodium bicarbonate solution. The resulting mixture was extracted twice with ethyl acetate. The combined organic extracts were washed with brine, dried over magnesium sulfate, filtered and evaporated carefully to give crude (2R)-2-hydroxybutanoic acid (6.57 g), which was used directly for the next step without further purification.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.03 (3H, t, J=7.5 Hz), 0.77 (1H, m), 1.90 (1H, m), 4.26 (1H, t, J=5 Hz);

MASS (ES-): m/e 103.

#### Preparation 115

25 To a stirred solution of crude (2R)-2-hydroxybutanoic acid (2.0 g) in a mixture of methanol (5 ml) and ether (15 ml) was added (trimethylsilyl)diazomethane (2.0 M in hexane, 9.6 ml) dropwise in an ice bath. The reaction mixture was stirred at ambient temperature overnight. The solvent was evaporated carefully to give crude methyl (2R)-2-hydroxybutanoate as a pale yellow oil (1.9 g), which was used directly for the next step without further purification.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.96 (3H, t, J=7.5 Hz), 1.70 (1H, m), 1.84 (1H, m), 3.80 (3H, s), 4.17 (1H, dd, J=7.5 Hz);

MASS (ES+): m/e 119.

#### Preparation 116

35 To a stirred solution of methyl (2R)-2-hydroxybutanoate (1.74 g) in N,N-dimethylformamide (15 ml) was added a solution of tert-

butyldiphenylchlorosilane (4.05 g) in N,N-dimethylformamide (5 ml) followed by imidazole (1.05 g) at ambient temperature. The resulting mixture was stirred at the same temperature for three hours and the reaction mixture was poured into ice water and extracted with ethyl acetate. The organic layer was washed with water and brine, and dried over magnesium sulfate. The organic layer was filtered and concentrated in vacuo to give crude methyl-(2R)-2-tert-butyl-  
5 butyldiphenylsilyloxybutanoate (5.11 g), which was used directly for the next step without further purification.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.91 (3H, t, J=7.5 Hz), 1.10 (3x3H, s), 1.74 (2H, dq, J=7.5, 5 Hz), 3.48 (3H, s), 4.20 (1H, t, J=5 Hz), 7.32-7.46 (6H, m), 7.59-7.75 (4H, m);  
MASS (ES+) m/e 357.

Preparation 117

15 To a stirred solution of dimethyl methylphosphonate (8.87 g) in tetrahydrofuran (50 ml) was added n-butyllithium (1.6 M in hexane, 45 ml) dropwise at -78°C over twenty minutes and the resulting mixture was stirred at the same temperature for half an hour. To this was added a solution of methyl (2R)-2-tert-butyl-  
20 butyldiphenylsilyloxybutanoate in tetrahydrofuran (30 ml) dropwise at the same temperature over twenty minutes. The mixture was stirred at the same temperature for two hours and allowed to warm to 0°C. The reaction mixture was poured into saturated ammonium chloride and extracted twice with ethyl acetate. The combined organic extracts were washed twice with water  
25 and brine, and dried over magnesium sulfate. The organic layer was filtered and concentrated in vacuo. The crude product was purified by flash chromatography eluting with 50% ethyl acetate /hexane (v/v) as a solvent mixture to give dimethyl (3R)-3-tert-butyl-  
30 butyldiphenylsilyloxy-2-oxopentylphosphate (3.06 g) as a pale yellow oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.5 Hz), 1.11 (3x3H, s), 1.63 (2H, m), 2.91 (1H, dd, J=22, 16 Hz), 3.35 (1H, dd, J=20, 16 Hz), 3.70 (3H, d, J=2 Hz), 3.74 (3H, d, J=2 Hz), 4.15 (1H, m), 7.32-7.48 (6H, m), 7.56-7.67 (4H, m);  
MASS (ES+) m/e 447.

35 Preparation 118

Compound (118) was obtained in a manner similar to Preparation

1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.41 (3x3H, s), 2.96 (2H, m), 4.50 (1H, m), 5.16 (1H, d, J=8.5 Hz), 6.54 (1H, d, J=7.5 Hz), 6.62-6.82 (2H, m);

MASS (ES-): m/e 296.

5 Preparation 119

To a stirred solution of (2S)-tert-butoxycarbonylamino-3-(3,4-dihydroxyphenyl)propanoic acid (13.66 g) in N,N-dimethylformamide (150 ml) was added potassium carbonate (22.9 g) at 0°C and the resulting mixture was stirred at the same temperature for half an hour. To this  
10 mixture was added methyl iodide (21.5 g) at the same temperature and the reaction mixture was left at ambient temperature for 2 days. The mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with water and brine, and dried over magnesium sulfate. The organic layer was filtered and concentrated in  
15 vacuo. The residue was purified by flash chromatography eluting with 25 to 50% ethyl acetate/hexane (v/v) as a solvent mixture to give pure methyl (2S)-2-tert-butoxycarbonylamino-3-(3,4-dimethoxyphenyl)-propanoate (7.17 g) as a brown oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.42 (3x3H, s), 3.01 (1H, dd, J=14, 5.5 Hz),  
20 3.06 (1H, dd, J=14, 5.5 Hz), 3.72 (3H, s), 3.86 (2x3H, s), 4.56 (1H, ddd, J=8.5, 5.5, 5.5 Hz), 4.97 (1H, brd, J=8.5 Hz), 6.64 (1H, s), 6.66 (1H, d, J=8 Hz), 6.79 (1H, d, J=8 Hz);

MASS (ES+) m/e 340.

Preparation 120

25 To a stirred solution of methyl (2S)-2-tert-butoxycarbonylamino-3-(3,4-dimethoxyphenyl)propanoate (7.13 g) in methanol (40 ml) was added 1 N sodium hydroxide (40 ml) at ambient temperature and the resulting mixture was stirred at the same temperature for three hours and a half. The solvent was evaporated  
30 under reduced pressure and the residue was dissolved in water and extracted with ether. The aqueous layer was separated, acidified to pH 2 with concentrated hydrochloric acid and extracted with ethyl acetate. The organic extract was washed with brine, dried over magnesium sulfate, filtered and concentrated in vacuo. The residue  
35 was triturated with 50% ether/hexane (v/v) to give (2S)-2-tert-butoxycarbonylamino-3-(3,4-dimethoxyphenyl)propanoic acid (5.35 g) as

a white amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.42 (3x3H, s), 3.04 (1H, dd, J=14 and 6 Hz), 3.13 (1H, dd, J=14 and 5.5 Hz), 3.855 (3H, s), 3.862 (3H, s), 4.56 (1H, m), 4.92 (1H, brd, J=7.5 Hz), 6.71 (1H, s), 6.72 (1H, d, J=8 Hz), 6.80 (1H, d, J=8 Hz);

MASS (ES+) m/e 324.

#### Preparation 121

To a stirred solution of tert-butyl (2R)-1-[(2S)-2-benzyloxycarbonylamino]-3-phenylpropanoylpyrrolidine-2-carboxylate (4.33 g) in methanol (40 ml) was added palladium on carbon (10%, 400 mg) and the mixture was stirred under 3 atm hydrogen atmosphere for eighteen hours. The reaction mixture was filtered through a Celite® pad. The filtrate was evaporated to give crude (1S)-1-benzyl-2-[(2R)-2-tert-butoxycarbonylpyrrolidin-1-yl]-2-oxoethylcarbamic acid (3.26 g) as an amorphous solid, which was used directly for the next step without further purification.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.30-2.20 (4H, m), 1.42 (9x4/5H, s), 1.48 (9x1/5H, s), 3.14 (1H, m), 3.37-3.77 (3H, m), 4.17 (1x4/5H, t, J=5 Hz), 4.41 (1x1/5H, br), 4.64 (1x4/5H, m), 4.89 (1x1/5H, m), 7.12-7.45 (5H, m), 8.39 (2x1/5H, br), 8.63 (2x4/5H, br);

MASS (ES+) m/e 319.

#### Preparation 122

Compound (122) was obtained in a manner similar to Preparation 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82-1.88 (13H, m), 1.45 (3x3H, s), 4.34 (1H, dt, J=8.5, 5 Hz), 4.86 (1H, d, J=8, 5 Hz);

MASS (ES-) m/e 270.

#### Preparation 123

Compound (123) was obtained in a manner similar to Preparation 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.38 (3x3H, s), 5.10 (1H, d, J=8 Hz), 7.25-7.43 (5H, m), 7.59 (1H, d, J=8 Hz);

MASS (ES-) m/e 250.

#### Preparation 124

Compound (124) was obtained in a manner similar to Preparation 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.96 (3H, d, J=7.0 Hz), 0.99 (3H, d, J=7.0 Hz), 1.41-1.49 (1H, m), 1.45 (9H, s), 1.47 (3H, s), 2.28 (1H, brs), 5.04 (1H, brs);  
MASS (ES+) m/e 232.10 (M+1).

5 Preparation 125

Compound (125) was obtained in a manner similar to Preparation 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.42 (9H, s), 3.21 (1H, s), 3.27 (1H, s), 3.66 (1H, s), 3.72 (1H, s), 5.13 (1H, brs), 7.16-7.28 (4H, m);  
10 MASS (ES-) m/e 276.12 (M-1).

Preparation 126

Compound (126) was obtained in a manner similar to Preparation 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 4.84-5.12 (1H, br), 2.19-2.34 (2H, m),  
15 1.70-2.04 (6H, m), 1.44 (9H, s), 1.28-1.49 (1H, m);  
MASS (ES+) m/e 230.14 (M+1).

Preparation 127

Compound (127) was obtained in a manner similar to Preparation 15.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, d, J=7.0 Hz), 0.91 (3H, d, J=7.0 Hz), 1.36-1.54 (1H, m), 1.41 (9H, s), 1.43 (3H, s), 1.72-1.96 (3H, m), 2.10-2.35 (1H, m), 2.58-2.68 (1H, m), 2.93 (1H, dd, J=12.8, 9.5 Hz), 3.11 (1H, dd, J=12.8, 5.1 Hz), 3.47-3.59 (1H, m), 4.35 (1H, dd, J=8.1, 4.0 Hz), 4.65-4.99 (2H, m), 5.06-5.22 (2H, m), 7.04-7.39 (11H, m);  
25 MASS (ES+) m/e 566.30 (M+1).

Preparation 128

Compound (128) was obtained in a manner similar to Preparation 16.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, d, J=6.9 Hz), 0.92 (3H, d, J=6.6 Hz), 1.08-1.99 (11H, m), 1.43 (9H, s), 1.46 (3H, s), 2.22-2.39 (1H, m), 2.72-2.90 (1H, m), 2.95-3.09 (1H, m), 3.52-3.61 (1H, m), 3.93-4.09 (1H, m), 4.30-4.39 (1H, m), 4.31 (2H, t, J=6.6 Hz), 4.69-4.76 (1H, m), 4.95 (1H, dt, J=8.4, 5.9 Hz), 5.10-5.23 (2H, m), 6.78 (1H, s), 7.05-7.37 (11H, m), 7.39-7.48 (2H, m), 7.51-7.61 (1H, m), 8.00-8.07 (2H, m);  
35 MASS (ES+) m/e 799.41 (M+1).

Preparation 129

Compound (129) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.55-0.70 (3H, m), 0.80-1.04 (3H, m), 1.29 (3H, s), 1.54-2.22 (12H, m), 2.46-2.62 (1H, m), 2.85-3.09 (2H, m),  
5 3.73-3.88 (1H, m), 4.00-4.39 (3H, m), 4.91-5.04 (1H, m), 7.14-7.31 (6H, m), 7.35-7.45 (2H, m), 7.47-7.57 (1H, m), 7.85 (1H, br), 7.95-8.05 (2H, m), 8.24 (2H, br);

MASS (ES+) m/e 609.3 (Free, M+1).

Preparation 130

10 Compound (130) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, d, J=7.0 Hz), 0.85 (3H, d, J=6.6 Hz), 1.14 (3H, s), 1.32-2.00 (9H, m), 2.10-2.40 (2H, m), 2.99 (1H, dd, J=13.9, 7.0 Hz), 3.20 (1H, dd, J=13.9, 8.8 Hz), 3.26-3.37 (1H, m),  
15 3.82-3.92 (1H, m), 4.18-4.29 (1H, m), 4.31 (2H, t, J=6.6 Hz), 4.65-4.71 (1H, m), 5.15-5.26 (1H, m), 5.75 (1H, s), 7.12 (1H, d, J=10.6 Hz), 7.15-7.31 (5H, m), 7.39-7.47 (2H, m), 7.52-7.62 (2H, m), 7.99-8.06 (2H, m);

MASS (ES+) m/e 591.37 (M+1).

20 Preparation 131

Compound (131) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, d, J=7.0 Hz), 0.88 (3H, d, J=6.6 Hz), 1.15 (3H, s), 1.22-1.94 (9H, m), 2.09-2.37 (2H, m), 2.99 (1H, dd, J=13.9, 7.0 Hz), 3.20 (1H, dd, J=13.9, 8.8 Hz), 3.26-3.37 (2H, m),  
25 3.65 (2H, t, J=6.2 Hz), 3.82-3.93 (1H, m), 4.17-4.28 (1H, m), 4.65-4.72 (1H, m), 5.15-5.26 (1H, m), 5.85 (1H, s), 7.12 (1H, d, J=10.3 Hz), 7.16-7.31 (5H, m), 7.58 (1H, d, J=10.3 Hz);

MASS (ES+) m/e 487.39 (M+1).

30 Preparation 132

Compound (132) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 62.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.71 (3H, d, J=7.0 Hz), 0.89 (3H, d, J=6.6 Hz), 1.15 (3H, s), 1.48-1.94 (6H, m), 2.09-2.41 (2H, m), 2.43-2.55 (2H, m), 2.99 (1H, dd, J=13.6, 7.0 Hz), 3.20 (1H, dd, J=13.6, 8.8 Hz),  
35 3.25-3.37 (2H, m), 3.89 (1H, dt, J=8.4, 4.8 Hz), 4.24 (1H, ddd, J=10.3,

7.3, 7.0 Hz), 4.66-4.72 (1H, m), 5.21 (1H, m), 7.53 (1H, d, J=10.3 Hz), 9.77 (1H, dd, J=1.1, 1.5 Hz);  
MASS (ES+) m/e 485.40 (M+1).

Preparation 133

5           Compound (133) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.35 (9H, s), 1.71-1.95 (3H, m), 2.52-2.61 (1H, m), 2.69 (1H, dd, J=12.8 and 9.5 Hz), 2.90 (1H, dd, J=12.8, 5.1 Hz), 3.02-3.20 (2H, m), 3.23-3.33 (1H, m), 3.43-3.61 (1H, m), 4.31 (1H, 10 dd, J=8.4, 4.3 Hz), 4.41-4.53 (1H, m), 4.90 (1H, dt, J=9.5, 5.1 Hz), 4.95-5.05 (1H, m), 5.08 (1H, d, J=12.5 Hz), 5.17 (1H, d, J=12.5 Hz), 6.68 (1H, d, J=7.3 Hz), 6.96-7.48 (13H, m), 7.63 (1H, s), 7, 74-7.82 (3H, m);  
MASS (ES+) m/e 650.50 (M+1).

15   Preparation 134

          Compound (134) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.13-1.29 (2H, m), 1.30-1.98 (8H, m), 1.39 (9H, s), 2.58-2.70 (1H, m), 2.71-3.00 (2H, m), 3.08-3.20 (1H, m), 20 3.21-3.35 (1H, m), 3.47-3.59 (1H, m), 3.97-4.17 (3H, m), 4.27-4.35 (1H, m), 4.79-4.95 (2H, m), 5.03-5.18 (1H, m), 5.09 (1H, d, J=12.5 Hz), 5.16 (1H, d, J=12.5 Hz), 6.74-6.92 (1H, m), 7.07-7.46 (16H, m), 7.50-7.59 (1H, m), 7.61 (1H, s), 7.72-7.79 (3H, m), 8.01 (2H, d, J=7.7 Hz);  
MASS (ES+) m/e 883.63 (M+1).

25   Preparation 135

          Compound (135) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09-2.11 (10H, m), 1.38 (9H, s), 2.60-2.73 (1H, m), 2.72-2.82 (1H, m), 2.83-2.96 (1H, m), 3.10-3.21 (1H, m), 30 3.24-3.39 (1H, m), 3.59-3.76 (1H, m), 3.99-4.14 (3H, m), 4.20-4.36 (1H, m), 4.71-4.95 (2H, m), 5.26-5.36 (1H, m), 7.05-7.15 (1H, m), 7.16-7.26 (5H, m), 7.27-7.34 (1H, m), 7.35-7.47 (4H, m), 7.50-7.64 (3H, m), 7.70-7.80 (3H, m), 7.97-8.06 (2H, m);  
MASS (ES+) m/e 793.47 (M+1).

35   Preparation 136

          Compound (136) was obtained in a manner similar to Preparation

18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83-1.91 (10H, m), 2.45-3.11 (4H, m), 3.14-3.32 (1H, m), 3.55-3.69 (1H, m), 3.75-3.94 (2H, m), 4.04-4.14 (1H, m), 4.18-4.34 (1H, m), 4.47-4.64 (1H, m), 5.11-5.25 (1H, m), 7.03-7.55 (14H, m), 7.62-7.81 (3H, m), 7.85-8.15 (4H, m), 8.38 (1H, br);

MASS (ES+) m/e 693.47 (free, M+1).

#### Preparation 137

Compound (137) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.18-1.53 (2H, m), 1.59-1.94 (3H, m), 2.06-2.40 (5H, m), 2.86 (1H, dd, J=13.2, 5.1 Hz), 3.01 (1H, dd, J=13.9, 7.0 Hz), 3.03-3.15 (1H, m), 3.18 (1H, dd, J=13.2, 10.6 Hz), 3.39 (1H, dd, J=13.9, 8.4 Hz), 3.90-4.00 (1H, m), 4.19-4.35 (1H, m), 4.25 (2H, t, J=6.6 Hz), 4.59-4.65 (1H, m), 4.81-4.91 (1H, m), 5.07 (1H, dt, J=10.6, 5.1 Hz), 6.33 (1H, d, J=9.9 Hz), 6.47 (1H, d, J=10.6 Hz), 7.13-7.29 (5H, m), 7.34 (1H, dd, J=8.4, 1.5 Hz), 7.37-7.49 (5H, m), 7.52-7.59 (1H, m), 7.67 (1H, s), 7.73-7.83 (3H, m), 7.99-8.05 (2H, m);

MASS (ES+) m/e 675.50 (M+1).

#### Preparation 138

Compound (138) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.20-1.89 (9H, m), 2.14-2.39 (2H, m), 2.85 (1H, dd, J=13.6 and 5.1 Hz), 3.00 (1H, dd, J=14.3 and 6.6 Hz), 3.04-3.13 (1H, m), 3.17 (1H, dd, J=13.6 and 10.6 Hz), 3.38 (1H, dd, J=14.3, 8.4 Hz), 3.57 (2H, t, J=6.2 Hz), 3.90-3.99 (1H, m), 4.28 (1H, dt, J=10.3, 7.7 Hz), 4.58-4.65 (1H, m), 4.80-4.90 (1H, m), 5.06 (1H, dt, J=10.6, 5.1 Hz), 6.39 (1H, d, J=9.9 Hz), 6.48 (1H, d, J=10.6 Hz), 7.12-7.28 (6H, m), 7.34 (1H, dd, J=10.3, 1.8 Hz), 7.41-7.50 (2H, m), 7.67 (1H, m), 7.73-7.83 (3H, m);

MASS (ES+) m/e 571.35 (M+1).

#### Preparation 139

Compound (139) was obtained in a manner similar to Preparation 78.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.45-1.88 (6H, m), 2.13-2.48 (4H, m), 2.86 (1H, dd, J=13.6, 5.1 Hz), 3.02 (1H, dd, J=14.3, 7.0 Hz), 3.06-3.16 (1H, m), 3.18 (1H, dd, J=13.6, 10.6 Hz), 3.40 (1H, dd, J=14.3, 8.4 Hz),

3.91-4.01 (1H, m), 4.29 (1H, dt, J=10.3, 7.0 Hz), 4.58-4.67 (1H, m),  
4.80-4.92 (1H, m), 5.07 (1H, dt, J=10.6, 5.1 Hz), 6.33 (1H, d, J=9.9  
Hz), 6.44 (1H, d, J=10.3 Hz), 7.13-7.29 (6H, m), 7.35 (1H, dd, J=8.4,  
1.5 Hz), 7.40-7.52 (2H m), 7.67 (1H, s), 7.74-7.85 (3H, m), 9.69 (1H,  
5 s);

MASS (ES+) m/e 569.35 (M+1).

Preparation 140

Compound (140) was obtained in a manner similar to Preparation  
15.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.36-1.54 (1H, m), 1.43 (9H, s), 1.71-1.98  
(3H, m), 2.55-2.66 (1H, m), 2.86-3.11 (3H, m), 3.44-3.62 (1H, m), 3.45-  
(2H, d, J=16.6 Hz), 3.76 (2H, d, J=16.6 Hz), 4.34-4.40 (1H, m), 4.98  
(1H, ddd, J=9.5, 8.8, 5.1 Hz), 5.04-5.14 (1H, m), 5.10 (1H, d, J=12.5  
Hz), 5.19 (1H, d, J=12.5 Hz), 7.07 (1H, d, J=8.8 Hz), 7.12-7.30 (8H,  
15 m), 7.30-7.40 (5H, m);

MASS (ES+) m/e 612.49 (M+1).

Preparation 141

Compound (141) was obtained in a manner similar to Preparation  
16.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.37 (6H, s), 1.43 (3H, s), 1.48-2.03 (10H,  
m), 2.66-2.78 (1H, m), 2.84-3.05 (2H, m), 3.13-3.26 (1H, m), 3.27-3.49  
(2H, m), 3.53-3.67 (2H, m), 3.92-4.06 (1H, m), 4.17-4.38 (3H, m),  
4.88-5.00 (1H, m), 5.07-5.27 (3H, m), 6.86-6.97 (1H, m), 7.09-7.37  
(15H, m), 7.38-7.47 (2H, m), 7.51-7.59 (1H, m), 7.98-8.06 (2H, m);

25 MASS (ES+) m/e 845.56 (M+1).

Preparation 142

Compound (142) was obtained in a manner similar to Preparation  
17.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.38 (6H, s), 1.45 (3H, s), 1.50-1.89 (8H,  
m), 1.88-2.19 (1H, m), 2.65-2.79 (1H, m), 2.95-3.34 (4H, m), 3.45-3.76  
(4H, m), 3.92-4.05 (1H, m), 4.17-4.39 (4H, m), 4.78-4.92 (1H, m),  
5.13-5.35 (1H, m), 7.00-7.32 (10H, m), 7.39-7.60 (4H, m), 7.98-8.07  
(2H, m);

MASS (ES+) m/e 755.32 (M+1).

35 Preparation 143

Compound (143) was obtained in a manner similar to Preparation

18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.17-1.46 (2H, m), 1.53-2.16 (8H, m), 2.86-3.14 (2H, m), 3.26-3.78 (6H, m), 4.03-4.32 (4H, m), 4.89-5.01 (1H, m), 7.00-7.31 (9H, m), 7.33-7.43 (2H, m), 7.47-7.55 (1H, m), 7.73 (1H,

5 brs), 7.94-8.14 (4H, m), 8.30 (1H, brs), 8.86 (1H, brs);

MASS (ES+) m/e 655.37 (free, M+1).

#### Preparation 144

Compound (144) was obtained in a manner similar to Preparation 76.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.30-1.58 (4H, m), 1.66-1.94 (6H, m), 2.10-2.39 (2H, m), 2.93 (1H, dd, J=13.2, 5.1 Hz), 3.09-3.21 (1H, m), 3.30 (1H, dd, J=13.2, 10.3 Hz), 3.61 (1H, d, J=16.5 Hz), 3.89-4.01 (1H, m), 3.94 (2H, d, J=16.5 Hz), 4.17-4.38 (3H, m), 4.63-4.69 (1H, m), 5.14 (1H, dt, J=10.3, 5.1 Hz), 6.31 (1H, s), 7.05-7.31 (9H, m), 7.37-7.57

15 (4H, m), 7.99-8.04 (2H, m);

MASS (ES+) m/e 637.30 (M+1).

#### Preparation 145

Compound (145) was obtained in a manner similar to Preparation 77.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.21-1.89 (9H, m), 2.08-2.39 (2H, m), 2.85 (1H, d, J=16.8 Hz), 2.93 (1H, dd, J=13.2, 5.1 Hz), 3.10-3.21 (1H, m), 3.30 (1H, dd, J=13.2, 10.3 Hz), 3.62 (1H, d, J=16.8 Hz), 3.63 (2H, t, J=6.2 Hz), 3.89-4.00 (1H, m), 3.97 (2H, d, J=16.8 Hz), 4.22 (1H, dt, J=10.3, 7.7 Hz), 4.64-4.70 (1H, m), 5.14 (1H, dt, J=10.3, 5.1 Hz),

25 6.51 (1H, s), 7.12-7.30 (10H, m), 7.52 (1H, d, J=10.3 Hz);

MASS (ES+) m/e 533.34 (M+1).

#### Preparation 146

Compound (146) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 68.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.46-1.87 (6H, m), 2.07-2.44 (2H, m), 2.46 (2H, dt, J=7.0, 1.5 Hz), 2.86 (1H, d, J=16.2 Hz), 2.92 (1H, dd, J=13.2, 5.1 Hz), 3.08-3.20 (1H, m), 3.29 (1H, dd, J=13.2, 10.6 Hz), 3.61 (1H, d, J=16.2 Hz), 3.87-4.00 (1H, m), 3.96 (2H, d, J=16.2 Hz), 4.23 (1H, ddd, J=10.3, 7.7, 7.0 Hz), 4.62-4.71 (1H, m), 5.14 (1H, dt, J=10.6, 5.1 Hz), 6.44 (1H, s), 7.13-7.31 (10H, m), 7.48 (1H, d, J=10.3 Hz), 9.73 (1H, t, J=1.5 Hz);

MASS (ES+) m/e 531.28 (M+1).

Preparation 147

Compound (147) was obtained in a manner similar to Preparation 14.

5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.18-1.51 (2H, m), 1.42 (9H, s), 1.57-1.83 (2H, m), 2.48-2.58 (1H, m), 3.11 (1H, dd, J=12.8, 9.5 Hz), 3.23 (1H, dd, J=12.8, 5.3 Hz), 3.41-3.52 (1H, m), 4.31-4.39 (1H, m), 4.72 (1H, dt, J=9.5, 5.3 Hz), 5.09 (1H, d, J=12.5 Hz), 5.19 (1H, d, J=12.5 Hz), 5.43 (1H, d, J=8.8 Hz), 7.26-7.39 (5H, m), 7.39-7.49 (2H, m), 7.66 (1H, s), 7.69-7.81 (4H, m);

MASS (ES+) m/e 503.38 (M+1).

Preparation 148

Compound (148) was obtained in a manner similar to Preparation 15.

15 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.3 Hz), 1.20-2.06 (3H, m), 1.36 (3H, s), 1.41 (2H, s), 1.44 (7H, s), 2.55-2.66 (1H, m), 3.12 (1H, dd, J=12.8, 9.2 Hz), 3.18-3.28 (1H, m), 3.23 (1H, dd, J=12.8, 5.1 Hz), 3.45-3.62 (2H, m), 4.33-4.39 (1H, m), 4.97-5.16 (2H, m), 5.09 (1H, d, J=12.5 Hz), 5.15 (1H, d, J=12.5 Hz), 6.90 (1H, d, J=8.4 Hz), 7.28-7.49 (8H, m), 7.67 (1H, s), 7.70-7.81 (4H, m);

MASS (ES+) m/e 602.46 (M+1).

Preparation 149

Compound (149) was obtained in a manner similar to Preparation 16.

25 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, t, J=7.3 Hz), 1.31-2.07 (11H, m), 1.43 (9H, s), 1.48 (3H, s), 2.13-2.32 (1H, m), 2.68-2.78 (1H, m), 3.17 (2H, d, J=7.3 Hz), 3.52-3.63 (1H, m), 4.00-4.12 (1H, m), 4.31 (2H, t, J=6.2 Hz), 4.35-4.40 (1H, m), 4.92-5.23 (4H, m), 6.73-6.92 (1H, m), 6.97 (1H, s), 7.24-7.49 (12H, m), 7.51-7.82 (3H, m), 8.00-8.06 (2H, m);

MASS (ES+) m/e 835.60 (M+1).

Preparation 150

Compound (150) was obtained in a manner similar to Preparation 17.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.76 (3H, t, J=7.0 Hz), 1.43 (9H, s), 1.58-1.98 (15H, m), 2.65-2.78 (1H, m), 3.04-3.28 (2H, m), 3.65-3.77 (1H, m),

4.05-4.15 (1H, m), 4.22-4.38 (3H, m), 4.93-5.05 (1H, m), 5.50-5.60 (1H, m), 6.81 (1H, s), 7.22-7.58 (7H, m), 7.65 (1H, s), 7.68-7.83 (3H, m), 7.98-8.05 (2H, m);

MASS (ES+) m/e 745.52 (M+1).

5 Preparation 151

Compound (151) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.59-0.74 (3H, m), 1.07-2.19 (13H, m), 1.37 (3H, s), 2.91-3.31 (3H, m), 3.65-3.78 (1H, m), 4.06-4.38 (4H, m),  
10 4.99-5.10 (1H, m), 7.21-7.54 (7H, m), 7.60-7.78 (4H, m), 7.94-8.02 (2H, m), 8.08-8.49 (3H, m);

MASS (ES+) m/e 645.57 (free, M+1).

Preparation 152

15 Compound (152) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.0 Hz), 1.28 (3H, s), 1.36-1.56 (2H, m), 1.62-1.99 (6H, m), 2.07-2.22 (2H, m), 2.22-2.41 (2H, m), 3.12 (1H, dd, J=13.6, 5.9 Hz), 3.18-3.30 (1H, m), 3.41 (1H, dd, J=13.6, 9.9 Hz), 3.81-3.92 (1H, m), 4.19-4.31 (1H, m), 4.32 (2H, t, J=6.2 Hz),  
20 4.61-4.68 (1H, m), 5.30 (1H, dt, J=9.9, 5.9 Hz), 5.91 (1H, s), 7.16 (1H, d, J=10.6 Hz), 7.35-7.49 (5H, m), 7.51-7.59 (1H, m), 7.64 (1H, d, J=9.9 Hz), 7.69 (1H, s), 7.73-7.83 (3H, m), 8.00-8.06 (2H, m);

MASS (ES+) m/e 627.44 (M+1).

Preparation 153

25 Compound (153) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.28-1.52 (2H, m), 1.29 (3H, s), 1.53-1.96 (7H, m), 2.08-2.25 (2H, m), 2.25-2.41 (2H, m), 3.13 (1H, dd, J=13.6, 5.9 Hz), 3.19-3.30 (1H, m), 3.42 (1H, dd, J=13.6, 9.9 Hz), 3.67 (2H, t, J=6.6 Hz), 3.82-3.92 (1H, m), 4.24 (1H, dt, J=10.3, 7.3 Hz), 4.61-4.68 (1H, m), 5.30 (1H, dt, J=9.9, 5.9 Hz), 5.95 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.35-7.50 (3H, m), 7.63 (1H, d, J=10.3 Hz), 7.69 (1H, s), 7.72-7.83 (3H, m);

MASS (ES+) m/e 523.38 (M+1).

35 Preparation 154

Compound (154) was obtained in a manner similar to Preparation

78. The obtained compound was used in Example 71.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.49-1.93 (6H, m), 2.08-2.23 (2H, m), 2.24-2.39 (2H, m), 2.45-2.55 (2H, m), 3.12 (1H, dd, J=13.6, 5.9 Hz), 3.18-3.29 (1H, m), 3.41 (1H, dd, J=13.6, 9.9 Hz), 3.82-3.93 (1H, m), 4.18-4.30 (1H, m), 4.61-4.68 (1H, m), 5.30 (1H, dt, J=9.9, 5.9 Hz), 5.87 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.37 (1H, dd, J=8.4, 1.8 Hz), 7.42-7.49 (2H, m), 7.57 (1H, d, J=10.3 Hz), 7.69 (1H, s), 7.74-7.83 (3H, m), 9.77 (1H, s);

MASS (ES+) m/e 521.33 (M+1).

10 Preparation 155

Compound (155) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40 (9H, s), 1.40-1.50 (1H, m), 1.71-1.96 (3H, m), 2.50-2.85 (3H, m), 2.95-3.28 (2H, m), 3.45-3.60 (1H, m), 3.72 (3H, s), 4.30 (1H, dd, J=7.3, 4.1 Hz), 4.39-4.51 (1H, m), 4.81-4.92 (1H, m), 5.00-5.20 (1H, m), 5.07 (1H, d, J=12.1 Hz), 5.14 (1H, d, J=12.1 Hz), 6.58 (1H, d, J=8.1 Hz), 6.88 (1H, s), 7.08-7.37 (13H, m), 7.63 (1H, d, J=8.1 Hz);

MASS (ES+) m/e 653.51 (M+1).

20 Preparation 156

Compound (156) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.26-1.97 (14H, m), 1.39 (9H, s), 2.53-2.78 (2H, m), 2.94-3.31 (2H, m), 3.49-3.62 (1H, m), 3.71 (3H, s), 3.94-4.05 (1H, m), 4.16-4.36 (2H, m), 4.67-4.84 (1H, m), 4.99-5.19 (1H, m), 5.06 (1H, d, J=12.5 Hz), 5.13 (1H, d, J=12.5 Hz), 6.62-6.77 (1H, m), 6.86 (1H, s), 7.01-7.46 (15H, m), 7.50-7.57 (1H, m), 7.64 (1H, d, J=7.7 Hz), 7.99-8.06 (2H, m);

MASS (ES+) m/e 886.62 (M+1).

30 Preparation 157

Compound (157) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.16-2.14 (12H, m), 1.38 (9H, s), 2.49-2.67 (2H, m), 2.73-2.85 (1H, m), 3.08-3.28 (2H, m), 3.53-3.72 (1H, m), 3.72 (3H, s), 3.86-3.97 (1H, m), 4.18-4.35 (3H, m), 4.43-4.59 (1H, m), 4.60-4.74 (1H, m), 5.46 (1H, brs), 6.91 (1H, s), 7.00-7.12 (3H, m),

7.15-7.32 (5H, m), 7.38-7.47 (2H, m), 7.51-7.61 (2H, m), 7.99-8.06 (2H, m);

MASS (ES+) m/e 796.59 (M+1).

Preparation 158

5           Compound (158) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.03-1.20 (2H, m), 1.36-1.96 (11H, m), 2.63-3.23 (6H, m), 3.65 (3H, s), 3.97-4.20 (3H, m), 4.41-4.55 (1H, m), 4.96-5.13 (1H, m), 7.01-7.31 (9H, m), 7.36-7.45 (2H, m), 7.46-7.57 (1H, m), 7.62-7.70 (1H, m), 7.88-8.24 (4H, m);

10       MASS (ES+) m/e 696.53 (free, M+1).

Preparation 159

          Compound (159) was obtained in a manner similar to Preparation 76.

15       <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.34-1.53 (2H, m), 1.63-1.95 (6H, m), 2.13-2.38 (2H, m), 2.86 (1H, dd, J=13.2, 5.5 Hz), 3.00 (1H, dd, J=14.2, 6.6 Hz), 3.04-3.22 (1H, m), 3.17 (1H, dd, J=13.2, 9.9 Hz), 3.35 (1H, dd, J=14.2, 11.0 Hz), 3.70 (3H, s), 3.87-4.06 (1H, m), 4.28 (2H, t, J=6.6 Hz), 4.29-4.37 (1H, m), 4.59-4.65 (1H, m), 4.78-4.88 (1H, m), 5.08 (1H, dt, J=11.0, 5.5 Hz), 6.42 (1H, d, J=9.9 Hz), 6.54 (1H, d, J=11.0 Hz), 6.87 (1H, s), 7.08-7.31 (9H, m), 7.40-7.49 (2H, m), 7.55 (1H, d, J=7.7 Hz), 7.59 (1H, d, J=7.7 Hz), 8.00-8.07 (2H, m);

20       MASS (ES+) m/e 678.40 (M+1).

Preparation 160

25           Compound (160) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.21-1.92 (9H, m), 2.10-2.39 (2H, m), 2.86 (1H, dd, J=14.7, 6.6 Hz), 2.99 (1H, dd, J=13.6, 5.5 Hz), 3.04-3.15 (1H, m), 3.17 (1H, dd, J=13.6, 10.6 Hz), 3.34 (1H, dd, J=14.7, 9.2 Hz), 3.62 (2H, t, J=6.2 Hz), 3.72 (3H, s), 3.91-4.01 (1H, m), 4.29 (1H, dt, J=10.3, 7.7 Hz), 4.59-4.65 (1H, m), 4.81 (1H, dt, J=9.2, 6.6 Hz), 5.08 (1H, dt, J=10.6, 5.5 Hz), 6.44 (1H, d, J=10.3 Hz), 6.48 (1H, d, J=10.6 Hz), 6.87 (1H, s), 7.08-7.31 (9H, m), 7.60 (1H, dd, J=8.1, 0.7 Hz);

30       MASS (ES+) m/e 574.42 (M+1).

35       Preparation 161

          Compound (161) was obtained in a manner similar to Preparation

78. The obtained compound was used in Example 74.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40-1.91 (5H, m), 2.14-2.40 (2H, m), 2.44 (2H, dt, J=6.6, 1.5 Hz), 2.86 (1H, dd, J=13.2, 10.6 Hz), 2.99 (1H, dd, J=14.7, 6.2 Hz), 3.04-3.15 (1H, m), 3.17 (1H, dd, J=13.2, 10.6 Hz),  
5 3.34 (1H, dd, J=14.7, 8.4 Hz), 3.73 (3H, s), 3.92-4.01 (1H, m), 4.29 (1H, dt, J=10.3, 7.3 Hz), 4.58-4.65 (1H, m), 4.81 (1H, dt, J=9.9, 6.2 Hz), 5.08 (1H, dt, J=10.6, 5.1 Hz), 6.33 (1H, d, J=10.3 Hz), 6.43 (1H, d, J=10.3 Hz), 6.87 (1H, s), 7.07-7.36 (9H, m), 7.60 (1H, s, J=7.7 Hz), 9.73 (1H, s);  
10 MASS (ES+) m/e 572.35 (M+1).

Preparation 162

Compound (162) was obtained in a manner similar to Preparation 14.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.43 (9H, s), 1.45-1.61 (1H, m), 1.76-2.00 (3H, m), 2.29 (3H, s), 2.63-2.75 (1H, m), 2.84-3.06 (2H, m), 3.48-3.66 (1H, m), 4.32-4.39 (1H, m), 4.56-4.66 (1H, m), 5.07-5.23 (2H, m), 5.33-5.42 (1H, m), 7.02-7.12 (4H, m), 7.30-7.39 (5H, m);  
15 MASS (ES+) m/e 467.38 (M+1).

Preparation 163

- 20 Compound (163) was obtained in a manner similar to Preparation 15.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.5 Hz), 1.38 (3H, s), 1.41 (3H, s), 1.43 (6H, s), 1.45-1.64 (2H, m), 1.75-2.14 (4H, m), 2.30 (3H, s), 2.69-2.84 (1H, m), 2.91 (1H, dd, J=13.2, 9.0 Hz), 3.03 (1H, dd, J=13.2, 5.7 Hz), 3.50-3.61 (1H, m), 4.34-4.40 (1H, m), 4.93 (1H, dt, J=9.0, 5.7 Hz), 5.04-5.24 (3H, m), 6.88 (1H, d, J=9.0 Hz), 6.93-7.13 (5H, m), 7.29-7.40 (5H, m);  
25 MASS (ES+) m/e 566.52 (M+1).

Preparation 164

- 30 Compound (164) was obtained in a manner similar to Preparation 16.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, t, J=6.6 Hz), 1.38-2.00 (13H, m), 1.44 (9H, s), 1.49 (3H, s), 2.30 (3H, s), 2.75-3.00 (2H, m), 3.53-3.64 (1H, m), 3.98-4.12 (1H, m), 4.32 (2H, t, J=6.6 Hz), 4.39 (1H, dd, J=8.2, 4.4 Hz), 4.85-4.96 (1H, m), 5.06-5.19 (3H, m), 6.67-6.82 (1H, m), 6.91-7.01 (1H, m), 7.04-7.11 (4H, m), 7.29-7.37 (5H, m), 7.39-7.47  
35

(2H, m), 7.51-7.60 (1H, m), 8.00-8.06 (2H, m);

MASS (ES+) m/e 799.47 (M+1).

#### Preparation 165

Compound (165) was obtained in a manner similar to Preparation

5 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=10.5 Hz), 1.45 (12H, s),  
1.46-1.96 (12H, m), 2.11-2.24 (1H, m), 2.32 (3H, s), 2.72-2.84 (1H, m),  
2.89-3.07 (2H, m), 3.65-3.76 (1H, m), 4.00-4.12 (1H, m), 4.26-4.40 (3H,  
m), 4.83-4.94 (1H, m), 5.38 (1H, brs), 6.78 (1H, s), 7.07-7.12 (4H, m),  
10 7.16-7.22 (1H, d, J=8.1 Hz), 7.40-7.48 (2H, m), 7.52-7.60 (1H, m),  
8.01-8.07 (2H, m);

MASS (ES+) m/e 709.38 (M+1).

#### Preparation 166

Compound (166) was obtained in a manner similar to Preparation

15 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.64-0.75 (3H, m), 1.37 (3H, s), 1.54-2.14  
(12H, m), 2.27 (3H, s), 2.81-3.07 (4H, m), 3.67-3.80 (1H, m), 4.17-  
4.37 (4H, m), 4.85-4.96 (1H, m), 7.00-7.12 (4H, m), 7.36-7.44 (2H, m),  
7.49-7.64 (2H, m), 7.97-8.04 (2H, m), 8.07-8.43 (3H, m);

20 MASS (ES+) m/e 609.40 (free, M+1).

#### Preparation 167

Compound (167) was obtained in a manner similar to Preparation

76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.36-  
25 1.57 (2H, m), 1.62-1.98 (5H, m), 2.06-2.40 (4H, m), 2.30 (3H, s), 2.92  
(1H, dd, J=13.6, 6.3 Hz), 3.15-3.33 (2H, m), 3.82-3.91 (1H, m), 4.25  
(1H, dt, J=10.5, 7.7 Hz), 4.32 (2H, t, J=6.3 Hz), 4.64-4.70 (1H, m),  
5.17 (1H, dt, J=10.5, 6.3 Hz), 5.85 (1H, s), 7.04-7.16 (5H, m), 7.15  
(1H, d, J=10.5 Hz), 7.40-7.48 (2H, m), 7.50-7.60 (2H, m), 8.01-8.06  
30 (2H, m);

MASS (ES+): m/e 591.56 (M+1).

#### Preparation 168

Compound (168) was obtained in a manner similar to Preparation

77.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.94 (9H, m),  
1.28 (3H, s), 2.07-2.40 (4H, m), 2.30 (3H, s), 2.91 (1H, dd, J=13.2,

6.2 Hz), 3.20 (1H, dd, J=13.2, 9.9 Hz), 3.22-3.32 (1H, m), 3.66 (2H, t, J=6.3 Hz), 3.81-3.91 (1H, m), 4.23 (1H, dt, J=10.3, 7.7 Hz), 4.63-4.70 (1H, m), 5.16 (1H, dt, J=10.3, 6.2 Hz), 5.93 (1H, s), 7.04-7.14 (4H, m), 7.14 (1H, d, J=9.9 Hz), 7.53 (1H, d, J=10.3 Hz);

5 MASS (ES+): m/e 487.46 (M+1).

Preparation 169

Compound (169) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.49-1.91 (6H, m), 2.08-2.39 (4H, m), 2.30 (3H, s), 2.45-2.54 (2H, t, J=6.3 Hz), 2.91 (1H, dd, J=13.6, 5.9 Hz), 3.20 (1H, dd, J=13.6, 10.3 Hz), 3.22-3.32 (1H, m), 3.81-3.91 (1H, m), 4.23 (1H, dt, J=10.6, 7.0 Hz), 4.64-4.70 (1H, m), 5.15 (1H, dt, J=10.3, 5.9 Hz), 5.87 (1H, s), 7.05-7.14 (4H, m), 7.15 (1H, d, J=10.6 Hz), 7.48 (1H, d, J=10.3 Hz), 9.77 (1H, s);

15 MASS (ES+): m/e 485.39 (M+1).

Preparation 170

Compound (170) was obtained in a manner similar to Preparation 14.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.32-1.38 (9H, m), 1.56-2.31 (3H, m), 3.01-3.23 (2H, m), 3.33-3.43 (1H, m), 3.57-3.80 (1H, m), 4.36-4.44 (1H, m), 4.84-4.96 (1H, m), 5.05-5.23 (3H, m), 5.35-5.43 (1H, m), 7.07-7.20 (2H, m), 7.27-7.40 (5H, m), 7.49-7.62 (1H, m), 8.46-8.56 (1H, m);

MASS (ES+): m/e 454.31 (M+1).

25 Preparation 171

Compound (171) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.763 (3H, t, J=6.3 Hz), 1.33-1.53 (2H, m), 1.36-1.40 (3H, m), 1.42 (9H, s), 1.73-2.37 (4H, m), 3.03-3.30 (2H, m), 30 3.35-3.87 (2H, m), 4.40-4.45 (1H, m), 5.06-5.29 (4H, m), 7.09-7.17 (2H, m), 7.20-7.24 (1H, m), 7.29-7.42 (5H, m), 7.52-7.64 (1H, m), 8.44-8.52 (1H, m);

MASS (ES+): m/e 553.39 (M+1).

Preparation 172

35 Compound (172) was obtained in a manner similar to Preparation 16.

MASS (ES+): m/e 786.49 (M+1).

Preparation 173

Compound (172) (crude compound) was purified by flash column chromatography (Silica gel column, eluting with 80 to 100% ethyl acetate/hexane (v/v) then 5% methanol/ethyl acetate (v/v)) to give Compound (173) (1.36 g) as an amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.62-0.75 (3H, m), 1.33-2.27 (12H, m), 1.43 (9H, s), 3.02-3.29 (3H, m), 3.41-3.86 (2H, m), 4.00-4.10 (1H, m), 4.27-4.34 (2H, m), 4.40-4.46 (1H, m), 5.10-5.25 (4H, m), 6.96-7.02 (1H, m), 7.05-7.19 (2H, m), 7.28-7.48 (9H, m), 7.50-7.77 (3H, m), 8.00-8.06 (2H, m), 8.44-8.52 (1H, m);

MASS (ES+): m/e 786.41 (M+1).

Preparation 174

Compound (174) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.61-0.73 (3H, m), 1.30-2.31 (16H, m), 1.43 (9H, s), 3.08-3.30 (3H, m), 3.35-3.58 (1H, m), 3.78-4.07 (2H, m), 4.23-4.46 (3H, m), 5.11-5.24 (1H, m), 6.90-7.04 (1H, m), 7.13-7.31 (2H, m), 7.37-7.73 (5H, m), 7.99-8.06 (2H, m), 8.45-8.52 (1H, m);

MASS (ES+): m/e 696.49 (M+1).

Preparation 175

Compound (175) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.55-2.45 (19H, m), 2.75-3.92 (6H, m), 4.15-4.41 (3H, m), 6.90-6.92 (1H, m), 7.08-7.31 (2H, m), 7.35-7.61 (5H, m), 7.88-8.42 (3H, m), 8.80-8.95 (2H, m);

MASS (ES+): m/e 596.14 (free, M+1).

Preparation 176

Compound (176) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.5 Hz), 1.29 (3H, s), 1.33-1.97 (8H, m), 2.02-2.43 (4H, m), 3.12 (1H, dd, J=15.0, 6.0 Hz), 3.52 (1H, dd, J=15.0, 9.0 Hz), 3.75-3.85 (1H, m), 3.87-3.98 (1H, m), 4.20-4.31 (1H, m), 4.31 (2H, t, J=6.8 Hz), 4.64-4.72 (1H, m), 5.58 (1H, dt, J=9.0, 6.0 Hz), 5.87 (1H, s), 7.05-7.30 (4H, m), 7.39-7.62 (4H, m), 8.02 (2H, d, J=7.5 Hz), 8.45 (1H, d, J=4.5 Hz);

MASS (ES+): m/e 578.45 (M+1).

Preparation 177

Compound (177) was obtained in a manner similar to Preparation 77.

5  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.84 (1H, t,  $J=7.2$  Hz), 1.21-1.97 (8H, m),  
1.29 (3H, s), 2.07-2.45 (4H, m), 3.12 (1H, dd,  $J=15.3$ , 6.0 Hz), 3.52  
(1H, dd,  $J=15.3$ , 10.5 Hz), 3.65 (2H, t,  $J=6.0$  Hz), 3.74-3.84 (1H, m),  
3.87-3.98 (1H, m), 4.25 (1H, dt,  $J=9.9$ , 7.8 Hz), 4.68 (1H, dd,  $J=7.8$ ,  
2.7 Hz), 5.58 (1H, dt,  $J=10.5$ , 5.7 Hz), 5.94-6.03 (1H, m), 7.06-7.13  
10 (1H, m), 7.14-7.24 (2H, m), 7.42-7.64 (2H, m), 8.07-8.13 (1H, m),  
8.42-8.48 (1H, m);

MASS (ES+): m/e 474.43 (M+1).

Preparation 178

Compound (178) was obtained in a manner similar to Preparation  
15 78. The obtained compound was used in Example 80.

$^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.85 (3H, t,  $J=7.3$  Hz), 1.30 (3H, s), 1.49-  
2.03 (8H, m), 2.09-2.44 (4H, m), 2.44-2.53 (2H, m), 3.12 (1H, dd,  
 $J=15.0$ , 5.4 Hz), 3.53 (1H, dd,  $J=15.0$ , 9.9 Hz), 3.74-3.85 (1H, m),  
3.88-3.99 (1H, m), 4.26 (1H, dt,  $J=10.5$ , 7.5 Hz), 4.69 (1H, dd,  $J=7.5$ ,  
20 2.4 Hz), 5.58 (1H, dt,  $J=9.9$ , 5.4 Hz), 5.94 (1H, m), 7.07-7.13 (1H, m),  
7.15-7.25 (2H, m), 7.42-7.50 (1H, m), 7.57 (1H, dt,  $J=7.5$ , 1.8 Hz),  
8.43-8.47 (1H, m), 9.77 (1H, t,  $J=1.5$  Hz);

MASS (ES+): m/e 472.44 (M+1).

Preparation 179

25 Compound (179) was obtained in a manner similar to Preparation  
77.

$^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.84 (3H, t,  $J=7.3$  Hz), 1.24-1.93 (8H, m),  
1.28 (3H, s), 2.06-2.24 (2H, m), 2.16 (3H, s), 2.24-2.41 (2H, m), 2.91  
(1H, dd,  $J=13.6$ , 5.9 Hz), 3.20 (1H, dd,  $J=13.6$ , 9.9 Hz), 3.21-3.33 (1H,  
30 m), 3.65 (2H, t,  $J=6.6$  Hz), 3.79-3.90 (1H, m), 4.17-4.29 (1H, m), 4.67  
(1H, brd,  $J=6.0$  Hz), 5.15 (1H, dt,  $J=9.9$ , 6.2 Hz), 6.00 (1H, s), 7.12  
(1H, d,  $J=9.9$  Hz), 7.18 (2H, d,  $J=8.4$  Hz), 7.40 (2H, d,  $J=8.4$  Hz),  
7.55 (1H, d,  $J=10.3$  Hz);

MASS (ES+): m/e 530.42 (M+1).

35 Preparation 180

Compound (180) was obtained in a manner similar to Preparation

78. The obtained compound was used in Example 83.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.33 (1H, m), 1.29 (3H, s), 1.47-1.92 (5H, m), 2.08-2.39 (4H, m), 2.16 (3H, s), 2.50 (2H, brt, J=6.6 Hz), 2.91 (1H, dd, J=13.6, 5.9 Hz), 3.18-3.33 (1H, m),  
5 3.20 (1H, dd, J=13.6, 9.9 Hz), 3.80-3.91 (1H, m), 4.16-4.30 (1H, m), 4.66 (1H, brd, J=6.7 Hz), 5.15 (1H, dt, J=10.1, 5.9 Hz), 5.90 (1H, s), 7.13 (1H, d, J=7.3 Hz), 7.15 (1H, s), 7.18 (2H, d, J=8.4 Hz), 7.40 (2H, d, J=8.4 Hz), 7.49 (1H, d, J=10.6 Hz);  
MASS (ES<sup>+</sup>): m/e 528.32 (M+1).

10 Preparation 181

Compound (181) was obtained in a manner similar to Preparation 13.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.07-1.31 (2H, m), 1.35 (4.5H, brs), 1.45 (4.5H, brs), 1.50-1.75 (3H, m), 2.10-2.32 (1H, m), 2.74-3.05 (1H, m),  
15 3.81-4.10 (1H, m), 4.75 (0.5H, brs), 4.95 (0.5H, brs), 5.05-5.25 (2H, m), 7.25-7.40 (5H, m);  
MASS (ES<sup>+</sup>): m/e 320.29 (M+1).

Preparation 182

Compound (182) was obtained in a manner similar to Preparation  
20 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.49-0.69 (1H, m), 1.05-1.29 (1H, m), 1.42 (9H, s), 1.30-1.77 (3H, m), 2.14-2.25 (1H, m), 2.89-3.19 (3H, m), 3.48-3.62 (1H, m), 4.84-5.01 (1H, m), 5.08-5.23 (2H, m), 5.25-5.33 (1H, m), 5.43 (1H, brd, J=8.1 Hz), 7.02-7.40 (10H, m);  
25 MASS (ES<sup>+</sup>): m/e 467.41 (M+1).

Preparation 183

Compound (183) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.54-0.72 (1H, m), 0.78 (2.1H, t, J=7.3 Hz),  
30 0.99 (0.9H, m, J=7.3 Hz), 1.07-1.25 (1H, m), 1.31-2.03 (5H, m), 1.40 (3H, s), 1.42 (9H, s), 2.15-2.26 (1H, m), 2.66-3.20 (3H, m), 3.51-3.60 (1H, m), 4.98-5.30 (3H, m), 6.87-6.96 (0.7H, m), 7.02-7.10 (0.3H, m), 7.13-7.40 (11H, m);  
MASS (ES<sup>+</sup>): m/e 566.46 (M+1).

35 Preparation 184

Compound (184) was obtained in a manner similar to Preparation

16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60-0.85 (1H, m), 0.70 (3H, t, J=7.3 Hz), 1.08-1.30 (2H, m), 1.33-2.00 (9H, m), 1.44 (12H, s), 2.18-2.41 (2H, m), 2.92-3.21 (3H, m), 3.56-3.68 (1H, m), 3.95-4.16 (1H, m), 4.32 (2H, t, J=6.6 Hz), 5.00-5.31 (4H, m), 6.79 (1H, brd, J=8.1 Hz), 6.99-7.08 (1H, m), 7.14-7.39 (6H, m), 7.40-7.48 (2H, m), 7.51-7.62 (1H, m), 8.00-8.08 (2H, m);

MASS (ES<sup>+</sup>): m/e 799.47 (M+1).

Preparation 185

10 Compound (185) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.59-0.78 (1H, m), 0.76 (3H, t, J=7.3 Hz), 1.17-2.07 (13H, m), 1.40 (3H, s), 1.43 (9H, s), 2.19-2.30 (1H, m), 2.86-3.20 (3H, m), 3.62-3.77 (1H, m), 3.96-4.09 (1H, m), 4.25-4.39 (2H, m), 5.13-5.25 (2H, m), 5.43 (1H, brs), 6.96 (1H, brs), 7.11-7.35 (6H, m), 7.39-7.49 (2H, m), 7.52-7.62 (1H, m), 8.00-8.08 (2H, m);

MASS (ES<sup>+</sup>): m/e 709.48 (M+1).

Preparation 186

20 Compound (186) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.50-0.91 (4H, m), 1.03-2.23 (13H, m), 1.40 (3H, brs), 2.82-3.34 (3H, m), 3.42-3.66 (1H, m), 3.70-4.10 (1H, m), 4.19-4.52 (2H, m), 4.60-4.86 (1H, m), 5.05-5.28 (1H, m), 7.07-7.32 (5H, m), 7.34-7.47 (2H, m), 7.48-7.59 (1H, m), 7.83-8.17 (2H, m);

25 MASS (ES<sup>+</sup>): m/e 609.44 (free, M+1).

Preparation 187

Compound (187) was obtained in a manner similar to Preparation 76.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.75 (3H, t, J=7.3 Hz), 1.20-2.16 (13H, m), 2.19-2.31 (1H, m), 2.93 (1H, dt, J=13.4, 2.6 Hz), 3.04 (1H, dd, J=13.9, 7.3 Hz), 3.21 (1H, dd, J=13.9, 8.1 Hz), 3.94-4.05 (1H, m), 4.19-4.32 (1H, m), 4.31 (2H, t, J=6.2 Hz), 5.00-5.07 (1H, m), 5.36 (1H, dt, J=10.3, 7.7 Hz), 6.05 (1H, s), 6.53 (1H, d, J=10.6 Hz), 7.16-7.32 (5H, m), 7.39-7.48 (2H, m), 7.49-7.60 (2H, m), 7.98-8.06 (2H, m);

35 MASS (ES<sup>+</sup>): m/e 591.49 (M+1).

Preparation 188

Compound (188) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.3 Hz), 1.18-2.34 (14H, m), 1.27 (3H, s), 2.93 (1H, dt, J=13.2, 2.6 Hz), 3.04 (1H, dd, J=13.9, 7.3 Hz), 3.21 (1H, dd, J=13.9, 7.7 Hz), 3.59-3.71 (2H, m), 4.00 (1H, brd, J=13.6 Hz), 4.20-4.32 (1H, m), 5.04 (1H, brd, J=6.2 Hz), 5.36 (1H, dt, J=10.3, 7.7 Hz), 6.16 (1H, s), 6.54 (1H, d, J=10.3 Hz), 7.15-7.32 (5H, m), 7.54 (1H, d, J=9.9 Hz);  
MASS (ES<sup>+</sup>): m/e 487.40 (M+1).

10 Preparation 189

Compound (189) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 86.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.3 Hz), 1.18-1.37 (1H, m), 1.29 (3H, s), 1.45-2.31 (1H, m), 2.47-2.56 (2H, m), 2.94 (1H, dt, J=13.5, 2.9 Hz), 3.04 (1H, dd, J=13.9, 7.3 Hz), 3.21 (1H, dd, J=13.9, 7.7 Hz), 3.98 (1H, brd, J=13.2 Hz), 4.18-4.31 (1H, m), 5.04 (1H, brd, J=6.2 Hz), 5.36 (1H, dt, J=9.7, 7.9 Hz), 5.98 (1H, s), 6.50 (1H, d, J=10.6 Hz), 7.15-7.32 (5H, m), 7.43 (1H, d, J=9.9 Hz), 9.76-9.79 (1H, m);  
MASS (ES<sup>+</sup>): m/e 485.33 (M+1).

20 Preparation 190

Compound (190) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.22-1.72 (6H, m), 1.28 (3H, s), 1.74-1.93 (2H, m), 2.08-2.41 (4H, m), 2.96 (1H, dd, J=13.9, 6.6 Hz), 2.99 (3H, s), 3.20 (1H, dd, J=13.9, 9.2 Hz), 3.25-3.37 (1H, m), 3.65 (2H, t, J=6.4 Hz), 3.79-3.91 (1H, m), 4.24 (1H, dt, J=10.3, 7.5 Hz), 4.70 (1H, brd, J=7.7 Hz), 5.15 (1H, dt, J=9.7, 6.4 Hz), 6.07 (1H, s), 6.65 (1H, brs), 7.10 (1H, d, J=9.3 Hz), 7.13 (2H, d, J=8.4 Hz), 7.22 (2H, d, J=8.4 Hz), 7.61 (1H, d, J=10.3 Hz);  
MASS (ES<sup>+</sup>): m/e 566.40 (M+1).

30 Preparation 191

Compound (191) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 90.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.51-1.91 (4H, m), 2.08-2.39 (6H, m), 2.50 (2H, brt, J=7.3 Hz), 2.91-2.99

(1H, m), 2.99 (3H, s), 3.20 (1H, dd, J=13.9, 9.2 Hz), 3.25-3.36 (1H, m), 3.80-3.91 (1H, m), 4.18-4.30 (1H, m), 4.69 (1H, brd, J=7.3 Hz), 5.09-5.21 (1H, m), 6.01 (1H, s), 6.59 (1H, s), 7.07-7.17 (3H, m), 7.22 (2H, d, J=8.4 Hz), 7.55 (1H, d, J=10.3 Hz);

5 MASS (ES+): m/e 564.41 (M+1).

Preparation 192

Compound (192) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.43 (9H, m), 1.46-1.59 (1H, m), 1.72-2.02 (3H, m), 2.69-2.84 (1H, m), 2.98 (1H, dd, J=13.0, 8.8 Hz), 3.10 (1H, dd, J=13.0, 5.5 Hz), 3.49-3.67 (1H, m), 4.38 (1H, dd, J=8.1, 3.7 Hz), 4.68 (1H, dt, J=8.8, 5.5 Hz), 4.99-5.24 (2H, m), 5.40 (1H, d, J=8.8 Hz), 7.23-7.60 (14H, m);

MASS (ES+): m/e 529.38 (M+1).

15 Preparation 193

Compound (193) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.4 Hz), 1.38 (1.5H, s), 1.41 (1.5H, s), 1.44 (9H, s), 1.70-2.09 (4H, m), 2.74-2.95 (1H, m), 2.99 (1H, dd, J=13.3, 9.6 Hz), 3.13 (1H, dd, J=13.3, 5.1 Hz), 3.51-3.66 (1H, m), 4.39 (1H, dd, J=7.6, 3.3 Hz), 4.93-5.04 (1H, m), 5.06-5.26 (2H, m), 6.90 (1H, d, J=7.6 Hz), 7.27-7.59 (14H, m);

MASS (ES+): m/e 628.50.

Preparation 194

25 Compound (194) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.58 (0.6H, t, J=7.3 Hz), 0.73 (2.4H, t, J=7.3 Hz), 1.42 (3H, s), 1.44 (9H, s), 1.48-2.03 (9H, m), 2.83-2.96 (1H, m), 2.99-3.14 (2H, m), 3.54-3.66 (1H, m), 3.93-4.15 (1H, m), 4.25-4.36 (2H, m), 4.40 (1H, dd, J=7.6, 3.3 Hz), 4.92-5.03 (1H, m), 5.06-5.21 (2H, m), 6.72-6.90 (1H, m), 6.98 (1H, s), 7.23-7.60 (19H, m), 7.99-8.06 (2H, m);

MASS (ES+): m/e 861.60 (M+1).

Preparation 195

35 Compound (195) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.3 Hz), 1.44 (12H, s), 1.46-2.21 (12H, m), 2.81-2.94 (1H, m), 3.00-3.11 (2H, m), 3.65-3.77 (1H, m), 3.96-4.10 (1H, m), 4.23-4.42 (3H, m), 4.97 (1H, q, J=8.1 Hz), 6.84 (1H, brs), 7.22-7.62 (13H, m), 7.98-8.07 (2H, m);

5 MASS (ES+): m/e 771.52 (M+1).

Preparation 196

Compound (196) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, brt, J=7.3 Hz), 1.39 (3H, s),  
10 1.54-2.21 (12H, m), 2.86-3.39 (3H, m), 3.67-3.82 (1H, m), 4.18-4.38 (4H, m), 4.91-5.05 (1H, m), 7.23-7.54 (12H, m), 7.72 (1H, brd, J=8.8 Hz), 7.99 (2H, d, J=7.0 Hz), 8.22 (2H, brs), 8.42 (1H, brs);  
MASS (ES+): m/e 671.53 (free, M+1).

Preparation 197

15 Compound (197) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.35-1.57 (2H, m), 1.64-2.00 (6H, m), 2.07-2.41 (4H, m), 3.01 (1H, dd, J=13.5, 6.3 Hz), 3.21-3.38 (2H, m), 3.81-3.95 (1H, m), 4.19-4.31 (1H,  
20 m), 4.32 (2H, t, J=6.4 Hz), 4.69 (1H, brd, J=5.9 Hz), 5.16-5.29 (1H, m), 5.93 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.27-7.36 (4H, m), 7.38-7.47 (4H, m), 7.48-7.63 (5H, m), 8.03 (2H, d, J=7.3 Hz);  
MASS (ES+): m/e 653.45 (M+1).

Preparation 198

25 Compound (198) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.30-1.95 (8H, m), 2.07-2.41 (4H, m), 3.01 (1H, dd, J=13.6, 6.3 Hz), 3.20-3.38 (2H, m), 3.66 (2H, t, J=6.3 Hz), 3.82-3.95 (1H, m), 4.18-4.31 (1H,  
30 m), 4.70 (1H, brd, J=5.9 Hz), 5.16-5.29 (1H, m), 5.97 (1H, s), 7.14 (1H, d, J=10.6 Hz), 7.24-7.65 (9H, m);  
MASS (ES+): m/e 549.47 (M+1).

Preparation 199

Compound (199) was obtained in a manner similar to Preparation  
35 78. The obtained compound was used in Example 93.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.30 (3H, s), 1.52-

- 1.94 (6H, m), 2.09-2.40 (4H, m), 2.51 (2H, brt, J=6.2 Hz), 3.01 (1H, dd, J=13.5, 6.2 Hz), 3.21-3.38 (2H, m), 3.83-3.95 (1H, m), 4.18-4.31 (1H, m), 4.69 (1H, brd, J=5.4 Hz), 5.16-5.29 (1H, m), 5.88 (1H, s), 7.14 (1H, d, J=10.2 Hz), 7.24-7.37 (3H, m), 7.38-7.47 (2H, m), 7.48-7.60 (5H, m), 9.78 (1H, s);
- 5 MASS (ES+): m/e 547.44 (M+1).

#### Preparation 200

Compound (200) was obtained in a manner similar to Preparation 14.

- 10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.44 (3x3H, s), 1.53 (1H, m), 1.75-2.00 (3H, m), 2.65 (1H, m), 2.88 (1H, dd, J=13, 10 Hz), 3.02 (1H, dd, J=13, 6 Hz), 3.53 (1H, m), 3.85 (2x3H, s), 4.36 (1H, dd, J=8, 4 Hz), 4.62 (1H, ddd, J=10, 8, 6 Hz), 5.11 (1H, d, J=12 Hz), 5.21 (1H, d, J=12 Hz), 5.38 (1H, d, J=8 Hz), 6.70-6.79 (3H, m), 7.28-7.40 (5H, m);
- 15 MASS (ES+): m/e 513.

#### Preparation 201

Compound (201) was obtained in a manner similar to Preparation 21.

- 20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.48 (1H, m), 1.70-1.90 (3H, m), 2.50 (1H, m), 3.11 (1H, m), 3.57 (1H, m), 3.72 (1H, m), 3.81 (3H, s), 3.84 (3H, s), 4.35 (1H, m), 4.66 (1H, m), 5.04 (1H, d, J=12 Hz), 5.13 (1H, d, J=12 Hz), 6.66-6.96 (3H, m), 7.22-7.37 (5H, m);
- MASS (ES+): m/e 413.

#### Preparation 202

- 25 Compound (202) was obtained in a manner similar to Preparation 22.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60 (3x1/7H, t, J=7.5 Hz), 0.81 (3x6/7H, t, J=7.5 Hz), 1.32 (3x1/7H, s), 1.39 (3x3x1/7H, s), 1.41 (3x6/7H, s), 1.43 (3x3x6/7H, s), 1.50-1.70 (2H, m), 1.76-2.02 (4H, m), 2.68 (1H, m), 2.88 (1H, dd, J=13.5, 9.5 Hz), 3.02 (1H, dd, J=13.5, 5 Hz), 3.56 (1H, m), 3.81 (3x1/7H, s), 3.82 (3x1/7H, s), 3.84 (3x6/7H, s), 3.85 (3x6/7H, s), 4.38 (1H, dd, J=8, 4 Hz), 4.92 (1H, ddd, J=9.5, 8.5 Hz), 5.11 (1H, d, J=12.5 Hz), 5.13 (1H, br), 5.15 (1H, d, J=12.5 Hz), 6.59-6.79 (3H, m), 6.88 (1H, d, J=8 Hz), 7.28-7.40 (5H, m);
- 30
- 35 MASS (ES+): m/e 612.

#### Preparation 203

Compound (203) was obtained in a manner similar to Preparation 23.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.46 (3x1/3H, t, J=7.5 Hz), 0.89 (3x2/3H, t, J=7.5 Hz), 1.40-2.33 (6H, m), 1.50 (3x1/3H, s), 1.66 (3x2/3H, s), 2.85 (1x2/3H, m), 2.93-3.18 (2H, m), 3.50-3.90 (1+1/3H, m), 3.81 (3x1/3H, s), 3.83 (3x2/3H, s), 3.84 (3x2/3H, s), 3.85 (3x1/3H, s), 4.33 (1x2/3H, m), 4.67 (1/1/3H, m), 4.94 (1x2/3H, m), 5.07-5.34 (2+1/3H, m), 6.65-7.06 (3H, m), 7.23-7.41 (5H, m), 7.67 (1x2/3H, J=8 Hz), 8.43 (1x1/3H, d, J=8 Hz);

10 MASS (ES+): m/e 512.

#### Preparation 204

Compound (204) was obtained in a manner similar to Preparation 24.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.63 (3x1/8H, t, J=7.5 Hz), 0.74 (3x7/8H, t, J=7.5 Hz), 1.35 (3x1/8H, s), 1.42 (3x3x1/8H, s), 1.44 (3x3x7/8H, s), 1.50 (3x7/8H, s), 2.76 (1H, m), 2.92 (1H, dd, J=13.5, 9 Hz), 2.98 (1H, dd, J=13.5, 5 Hz), 3.57 (1H, m), 3.81 (2x3x1/8H, s), 3.84 (2x3x7/8H, s), 4.07 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.38 (1H, dd, J=8.4 Hz), 4.91 (1H, m), 5.13 (2H, s), 5.13 (1H, br), 6.59-6.83 (4H, m), 6.97 (1H, s), 7.28-7.40 (5H, m), 7.42 (2x1H, dd, J=7.5, 7.5 Hz);

20 MASS (ES+): m/e 845.

#### Preparation 205

Compound (205) was obtained in a manner similar to Preparation 25.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.5 Hz), 1.36-2.24 (12H, m), 1.44 (3x4H, s), 2.78 (1H, m), 2.97 (2H, d, J=7 Hz), 3.67 (1H, m), 3.80 (2x3H, s), 4.27-4.41 (3H, m), 4.91 (1H, dt, J=7.5, 7 Hz), 5.23 (1H, br), 6.71-6.80 (3H, m), 6.83 (1H, s), 7.28 (1H, d, J=7.5 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dd, J=7.5, 7.5 Hz), 8.03 (2x1H, d, J=7.5 Hz);

30 MASS (ES+): m/e 753.

#### Preparation 206

Compound (206) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.73 (3H, brt, J=7 Hz), 1.40 (3H, s), 1.54-2.17 (12H, m), 2.80-3.08 (3H, m), 3.76 (1H, m), 3.81 (3H, s), 3.83 (3H,

s), 4.20-4.40 (4H, m), 4.92 (1H, m), 6.68-6.82 (3H, m), 7.40 (2x1H, dd, J=7.5, 7.5 Hz), 7.53 (1H, dd, J=7.5, 7.5 Hz), 7.66 (1H, brd, J=7 Hz), 8.00 (2x1H, d, J=7.5 Hz), 8.21 (2H, br), 8.36 (1H, br);

MASS (ES-): m/e 653.

5 Preparation 207

Compound (207) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.47 (2H, m), 1.56-2.00 (6H, m), 2.06-2.40 (4H, m), 2.90 (1H, dd, J=13.5, 6 Hz), 3.20 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (2x3H, s), 3.86 (1H, m), 4.24 (1H, dt, J=10, 7.5 Hz), 4.32 (2H, t, J=6.5 Hz), 4.67 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.88 (1H, s), 6.75-6.80 (3H, m), 7.14 (1H, d, J=10 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52-7.60 (2H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

15 MASS (ES+): m/e 637.

Preparation 208

Compound (208) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.46 (2H, m), 1.62-2.06 (6H, m), 2.08-2.40 (4H, m), 2.90 (1H, dd, J=13.5, 6 Hz), 3.08-3.33 (2H, m), 3.85 (2x3H, s), 3.85 (1H, m), 4.24 (1H, m), 4.32 (1H, t, J=6.5 Hz), 4.67 (1H, m), 5.15 (1H, m), 5.91 (1H, s), 6.74-6.80 (3H, m), 7.15 (1H, d, J=10 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52-7.62 (2H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

25 MASS (ES-): m/e 635.

Preparation 209

Compound (209) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.30-1.53 (2H, m), 1.54-1.94 (6H, m), 2.07-2.40 (4H, m), 2.90 (1H, dd, J=13.5, 6 Hz), 3.19 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.66 (2H, t, J=6.5 Hz), 3.85 (2x3H, s), 3.85 (1H, m), 4.22 (1H, dt, J=10, 7.5 Hz), 4.67 (1H, m), 5.15 (1H, ddd, J=10, 10, 6 Hz), 5.97 (1H, s), 6.74-6.80 (3H, m), 7.14 (1H, d, J=10 Hz), 7.55 (1H, d, J=10 Hz);

35 MASS (ES-): m/e 531.

Preparation 210

Compound (210) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.5 Hz), 1.24-1.51 (2H, m), 1.29 (3H, s), 1.53-1.93 (6H, m), 2.08-2.40 (4H, m), 2.90 (1H, dd, J=13.5, 6 Hz), 3.19 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.66 (2H, t, J=6.5 Hz), 3.85 (2x3H, s), 3.86 (1H, m), 4.23 (1H, dt, J=10, 7.5 Hz), 4.68 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 6.03 (1H, s), 6.74-6.80 (3H, m), 7.15 (1H, d, J=10 Hz), 7.56 (1H, d, J=10 Hz);  
MASS (ES-): m/e 531.

10 Preparation 211

Compound (211) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 96.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 1.30 (3H, s), 1.50-1.92 (6H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 2.90 (1H, dd, J=13.5, 6 Hz), 3.19 (1H, dd, J=13.5, 9.5 Hz), 3.25 (1H, m), 3.85 (2x3H, s), 3.86 (1H, m), 4.23 (1H, dt, J=10, 7.3 Hz), 4.67 (1H, dd, J=8, 2.5 Hz), 5.15 (1H, ddd, J=10, 9.5, 6 Hz), 5.93 (1H, s), 6.73-6.80 (3H, m), 7.16 (1H, d, J=10 Hz), 7.50 (1H, d, J=10 Hz), 9, 77 (1H, t, J=1 Hz);  
MASS (ES-): m/e 529.

20 Preparation 212

Compound (212) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.74 (3x1/7H, d, J=7 Hz), 0.80 (3x1/7H, t, J=7 Hz), 0.89 (3x6/7H, t, J=7 Hz), 0.94 (3x6/7H, d, J=7 Hz), 1.12 (1H, m), 1.38-1.80 (3H, m), 1.42 (9x1/7H, s), 1.44 (9x6/7H, s), 1.88-2.26 (3H, m), 3.57 (1H, m), 3.90 (1H, m), 4.36 (1H, dd, J=9, 7 Hz), 4.49 (1H, dd, J=8, 3 Hz), 5.13 (1H, d, J=12.5 Hz), 5.19 (1H, d, J=9 Hz), 5.20 (1H, d, J=12.5 Hz), 7.28-7.41 (5H, m);  
MASS (ES+): m/e 419.

30 Preparation 213

Compound (213) was obtained in a manner similar to Preparation 21.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3x1/7H, t, J=7.3 Hz), 0.75 (3x1/7H, d, J=7 Hz), 0.86 (3x6/7H, t, J=7.3 Hz), 0.98 (3x6/7H, d, J=7 Hz), 1.13 (1H, m), 1.43 (1H, m), 1.76-2.02 (4H, m), 2.18 (1H, m), 3.52 (1H, m), 3.79 (1H, m), 4.13 (1H, m), 4.41 (1H, m), 5.10 (1x6/7H, d, J=12.5 Hz),

5.12 (1x1/7H, d, J=12.5 Hz), 5.19 (1x6/7H, d, J=12.5 Hz), 5.22 (1x1/7H, d, J=12.5 Hz), 7.30-7.44 (5H, m), 8.20 (2x6/7H, br), 8.32 (2x1/7H, br);

MASS (ES+): m/e 319.

5 Preparation 214

Compound (214) was obtained in a manner similar to Preparation 22.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.74 (3x1/5H, d, J=6.5 Hz), 0.79 (3H, t, J=7.5 Hz), 0.80 (3x1/5H, t, J=7.5 Hz), 0.87 (3x4/5H, t, J=7.5 Hz),  
10 0.94 (3x4/5H, d, J=6.5 Hz), 1.11 (1H, m), 1.39 (3H, s), 1.41 (9x1/5H, s), 1.43 (9x4/5H, s), 1.52-2.24 (8H, m), 3.57 (1H, m), 3.92 (1H, m), 4.32 (1x1/5H, dd, J=9.5, 7.5 Hz), 4.49 (1H, dd, J=8, 3 Hz), 4.68 (1H, dd, J=9.5, 7.5 Hz), 5.13 (2H, s), 5.14 (1H, br), 6.58 (1x1/5H, d, J=9.5 Hz), 6.67 (1x4/5H, d, J=9.5 Hz), 7.24-7.40 (5H, m);

15 MASS (ES+): m/e 518.

Preparation 215

Compound (215) was obtained in a manner similar to Preparation 23.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.71 (3x1/3H, d, J=6.5 Hz), 0.77 (3x1/3H, t, J=7 Hz), 0.82-0.99 (7H, m), 0.99-2.22 (9H, m), 1.63 (3x1/3H, s), 1.69 (3x2/3H, s), 3.56 (1H, m), 4.04 (1H, m), 4.28 (1x1/3H, dd, J=9.8 Hz), 4.46 (1H, dd, J=8.3 Hz), 4.63 (1x2/3H, dd, J=9, 8 Hz), 5.09-5.27 (2H, m), 7.25-7.40 (5H, m), 7.49 (1x2/3H, d, J=8 Hz), 8.05 (1x1/3H, d, J=8 Hz);

25 MASS (ES+): m/e 418.

Preparation 216

Compound (216) was obtained in a manner similar to Preparation 24.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.66-0.97 (9x1/5H, m), 0.72 (3x4/5H, t, J=7.3 Hz), 0.87 (3x4/5H, t, J=7.4 Hz), 0.93 (3x4/5H, d, J=6.7 Hz),  
30 1.00-2.45 (15H, m), 1.43 (3x3H, s), 1.50 (3x1/5H, s), 1.54 (3x4/5H, s), 3.57 (1H, m), 3.90 (1H, m), 4.08 (1H, m), 4.25-4.36 (2H, m), 4.59 (1H, dd, J=8, 3 Hz), 4.68 (1H, dd, J=9, 8 Hz), 5.02-5.24 (3H, m), 6.54 (1H, d, J=9 Hz), 6.91 (1x1/5H, s), 7.07 (1x4/5H, s), 7.27-7.47 (7H,  
35 m), 7.55 (1H, m), 8.02 (2x1H, d, J=7 Hz);

MASS (ES+): m/e 751.

Preparation 217

Compound (217) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.4 Hz), 0.88 (3H, t, J=7.3 Hz), 0.91 (3H, d, J=7.0 Hz), 1.04-2.38 (15H, m), 3.56 (1H, m), 3.92-4.12 (2H, m), 4.26-4.38 (2H, m), 4.50 (1H, m), 4.60 (1H, dd, J=9, 8 Hz), 5.28 (1H, br), 6.96 (1H, brs), 7.15 (1H, brd, J=9 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

10 MASS (ES-): m/e 659.

Preparation 218

Compound (218) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78-0.94 (9H, m), 1.02-2.22 (15H, m), 1.42 (3H, s), 3.52 (1H, m), 3.96 (1H, m), 4.20-4.40 (4H, m), 4.56 (1H, dd, J=9.8 Hz), 7.35-7.57 (4H, m), 8.01 (2x1H, d, J=7.5 Hz), 8.13 (2H, br), 8.36 (1H, brs);

MASS (ES+): m/e 561.

Preparation 219

20 Compound (219) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7 Hz), 0.87 (3H, d, J=7 Hz), 0.91 (3H, t, J=7 Hz), 1.17 (2H, m), 1.29 (3H, s), 1.34-2.10 (9H, m), 2.11-2.42 (4H, m), 3.52 (1H, dt, J=10, 7.5 Hz), 3.89 (1H, ddd, J=10, 8.5, 5 Hz), 4.24 (1H, dt, J=10.5, 7.5 Hz), 4.31 (2H, t, J=7 Hz), 4.56 (1H, dd, J=10.5, 10.5 Hz), 4.77 (1H, dd, J=8, 2 Hz), 5.86 (1H, s), 7.19 (1H, d, J=10.5 Hz), 7.37 (1H, d, J=10.5 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.02 (2x1H, dd, J=7.5, 1 Hz);

MASS (ES+): m/e 543.

30 Preparation 220

Compound (220) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, d, J=7 Hz), 0.88 (3H, t, J=7 Hz), 0.91 (3H, t, J=7 Hz), 1.08-1.51 (4H, m), 1.30 (3x3H, s), 1.53-1.76 (3H, m), 1.77-2.11 (4H, m), 2.13-2.43 (4H, m), 3.52 (1H, dt, J=10, 7.5 Hz), 3.65 (2H, t, J=7 Hz), 3.89 (1H, ddd, J=10, 8.5, 5 Hz), 4.23 (1H,

dt, J=10, 7.5 Hz), 4.58 (1H, dd, J=10.5, 10.5 Hz), 4.76 (1H, dd, J=7.5, 2 Hz), 6.01 (1H, s), 7.20 (1H, d, J=10 Hz), 7.38 (1H, d, J=10.5 Hz);

MASS (ES-): m/e 437.

5 Preparation 221

Compound (221) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 99.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, d, J=7 Hz), 0.88 (3H, t, J=7 Hz), 0.91 (3H, t, J=7 Hz), 1.17 (2H, m), 1.31 (3H, s), 1.50-1.75 (3H, m),  
10 1.74-2.10 (4H, m), 2.14-2.44 (4H, m), 2.49 (2H, m), 3.52 (1H, dt, J=10, 7.5 Hz), 3.89 (1H, ddd, J=10, 8.5, 4.5 Hz), 4.23 (1H, dt, J=10, 7 Hz), 4.58 (1H, dd, J=10.5, 10.5 Hz), 4.78 (1H, dd, J=8, 2 Hz), 5.91 (1H, s), 7.20 (1H, d, J=10 Hz), 7.31 (1H, d, J=10 Hz), 9.77 (1H, t, J=1 Hz);

15 MASS (ES-): m/e 435.

Preparation 222

Compound (222) was obtained in a manner similar to Preparation 22.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.69 (3x1/5H, t, J=7 Hz), 0.71 (3x1/5H, d, J=7 Hz), 0.81 (3x4/5H, t, J=7 Hz), 0.87 (3x4/5H, d, J=7 Hz), 1.32-1.78 (4H, m), 1.39 (3x3H, s), 1.88-2.26 (3H, m), 2.82-3.10 (2H, m), 3.56 (1H, m), 3.77 (3x4/5H, s), 3.80 (3x1/5H, s), 3.92 (1H, m), 4.35 (1H, m), 4.48 (1H, dd, J=8, 3 Hz), 4.67 (1H, dd, J=9, 7 Hz), 4.94 (1H, m), 5.13 (1x4/5H, d, J=12.5 Hz), 5.15 (1x1/5H, d, J=12 Hz), 5.19 (1x4/5H, d, J=12.5 Hz), 5.21 (1x1/5H, d, J=12 Hz), 6.56 (1H, brd, J=9 Hz), 6.81 (2x1/5H, d, J=8.5 Hz), 6.84 (2x4/5H, d, J=8.5 Hz), 7.06 (2x1/5H, d, J=8.5 Hz), 7.10 (2x4/5H, d, J=8.5 Hz), 7.29-7.42 (5H, m);

MASS (ES+): m/e 596.

Preparation 223

30 Compound (223) was obtained in a manner similar to Preparation 23.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.49-0.60 (2H, m), 0.69-0.79 (4H, m), 0.79-0.98 (2H, m), 1.25 (1H, m), 1.66 (1H, m), 1.76-2.00 (2H, m), 2.17 (1H, m), 2.82-2.96 (1+1/3H, m), 3.04 (1x2/3H, dd, J=14, 6 Hz), 3.60 (1H, m), 3.70 (1H, m), 3.72 (3x1/3H, s), 3.73 (3x2/3H, s), 3.95 (1x1/3H, dd, J=9, 8 Hz), 4.00 (1x1/3H, m), 4.11 (1x2/3H, m), 4.36 (1H, dd,

J=8.5, 3.5 Hz), 4.52 (1x2/3H, dd, J=9, 8 Hz), 5.09 (1x2/3H, d, J=12.5 Hz), 5.12 (1x1/3H, d, J=12.5 Hz), 5.13 (1x2/3H, d, J=12.5 Hz), 5.24 (1x1/3H, d, J=12.5 Hz), 6.87 (2x1/3H, d, J=8.5 Hz), 6.90 (2x2/3H, d, J=8.5 Hz), 7.16 (2x1/3H, d, J=8.5 Hz), 7.24 (2x2/3H, d, J=8.5 Hz),  
5 7.30-7.44 (5H, m), 8.20 (2H, br), 8.73 (1x2/3H, d, J=9 Hz), 8.82 (1x1/3H, d, J=9 Hz);

MASS (ES+): m/e 496.

#### Preparation 224

Compound (224) was obtained in a manner similar to Preparation  
10 24.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.64 (3x/6H, d, J=7 Hz), 0.68 (3x1/6H, t, J=7 Hz), 0.79 (3x5/6H, t, J=7 Hz), 0.84 (3x5/6H, d, J=7 Hz), 1.18-2.24 (13H, m), 3.00 (2H, m), 3.55 (1H, m), 3.75 (3H, s), 3.90 (1H, m), 4.08 (1H, m), 4.25 (2H, brt, J=7 Hz), 4.47 (1H, dd, J=8, 2 Hz), 4.56-4.71 (2H, m), 5.10 (1x5/6H, d, J=12.5 Hz), 5.14 (1x1/6H, d, J=12.5 Hz),  
15 5.18 (1x5/6H, d, J=12.5 Hz), 5.21 (1x1/6H, d, J=12.5 Hz), 5.23 (1H, m), 6.45 (1H, brd, J=9 Hz), 6.67 (1H, d, J=8 Hz), 6.79 (2x1/6H, d, J=8.5 Hz), 6.81 (2x5/6H, d, J=8.5 Hz), 7.07 (2x1/6H, d, J=8.5 Hz), 7.11 (2x5/6H, d, J=8.5 Hz), 7.28-7.46 (7H, m), 7.54 (1H, m), 8.02 (2x/1H, d, J=7.5 Hz);  
20

MASS (ES+): m/e 829.

#### Preparation 225

Compound (225) was obtained in a manner similar to Preparation  
17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7 Hz), 0.84 (3H, d, J=6 Hz), 1.16-2.24 (13H, m), 2.90-3.10 (2H, m), 3.54 (1H, m), 3.74 (3H, s), 3.92-4.19 (2H, m), 4.28 (2H, m), 4.40-4.52 (2H, m), 4.65 (1H, m), 5.40 (1H, brd, J=7.5 Hz), 6.78 (2x1H, d, J=8.5 Hz), 6.86 (1H, brd, J=8 Hz), 6.94 (1H, brd, J=8 Hz), 7.11 (2x1H, brd, J=8.5 Hz), 7.42 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, dd, J=7.5, 7.5 Hz), 8.02 (2x1H, d, J=7.5 Hz);  
30

MASS (ES-): m/e 737.

#### Preparation 226

Compound (226) was obtained in a manner similar to Preparation  
35 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.74 (3H, t, J=7 Hz), 0.88 (3H, d, J=6.5

Hz), 1.02 (1H, m), 1.20-1.46 (4H, m), 1.60-2.18 (8H, m), 2.91 (1H, dd, J=13.5, 8 Hz), 3.08 (1H, dd, J=13.5, 6.5 Hz), 3.48 (1H, m), 3.96 (1H, m), 4.14-4.35 (5H, m), 5.03 (1H, m), 6.67 (2x1H, d, J=8.5 Hz), 7.26 (2x1H, d, J=8.5 Hz), 7.40 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, dd, J=7.5, 7.5 Hz), 8.02 (2x1H, d, J=7.5 Hz), 8.04 (2H, br), 8.20 (1H, br), 8.47 (1H, br);  
MASS (ES-): m/e 637.

#### Preparation 227

Compound (227) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, d, J=7 Hz), 0.86 (3H, t, J=7 Hz), 1.09 (1H, m), 1.31-2.02 (10H, m), 2.24-2.46 (6H, m), 2.78 (1H, dd, J=14, 7.5 Hz), 3.15 (1H, dd, J=14, 7.5 Hz), 3.51 (1H, m), 3.76 (3H, s), 4.02 (1H, m), 4.22-4.34 (3H, m), 4.48 (1H, dd, J=10.5, 10.5 Hz), 4.64-4.76 (2H, m), 6.25 (1H, d, J=10 Hz), 6.28 (1H, d, J=10.5 Hz), 6.79 (2x1H, d, J=8.5 Hz), 7.11 (2x1H, d, J=8.5 Hz), 7.22 (1H, d, J=10 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.02 (2x1H, dd, J=7.5, 1.5 Hz);  
MASS (ES-): m/e 619.

#### Preparation 228

Compound (228) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, d, J=6.5 Hz), 0.86 (3H, t, J=7 Hz), 1.10 (1H, m), 1.22-2.02 (10H, m), 2.24-2.46 (2H, m), 2.79 (1H, dd, J=14.5, 7.5 Hz), 3.15 (1H, dd, J=14.5, 7.5 Hz), 3.51 (1H, m), 3.61 (2H, brt, J=6 Hz), 3.78 (3H, s), 4.02 (1H, m), 4.27 (1H, dt, J=10, 7.5 Hz), 4.48 (1H, dd, J=10.5, 10 Hz), 4.64-4.76 (2H, m), 6.31 (1H, d, J=10.5 Hz), 6.38 (1H, d, J=10 Hz), 6.81 (2x1H, d, J=8.5 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.22 (1H, d, J=10 Hz);  
MASS (ES-): m/e 515.

#### Preparation 229

Compound (229) was obtained in a manner similar to Preparation 78.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=6.6 Hz), 0.86 (3H, t, J=7.3 Hz), 1.09 (1H, m), 1.20-2.02 (10H, m), 2.24-2.46 (2H, m), 2.79 (1H, dd, J=14.3, 7.9 Hz), 3.15 (1H, dd, J=14.3, 7.3 Hz), 3.51 (1H, m), 3.61

(2H, t, J=6.4 Hz), 3.78 (3H, s), 4.02 (1H, m), 4.27 (1H, dt, J=10.3, 7.6 Hz), 4.48 (1H, dd, J=11.0, 10.5 Hz), 4.69 (1H, ddd, J=9.9, 7.9, 7.3 Hz), 4.72 (1H, dd, J=8.0, 2.0 Hz), 6.31 (1H, d, J=10.5 Hz), 6.37 (1H, d, J=9.9 Hz), 6.81 (2x1H, d, J=8.4 Hz), 7.12 (2x1H, d, J=8.4 Hz),  
5 7.22 (1H, d, J=10.3 Hz);

MASS (ES-): m/e 515.

#### Preparation 230

Compound (230) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 102.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, d, J=6.6 Hz), 0.87 (3H, t, J=7.3 Hz), 1.10 (1H, m), 1.44-2.06 (8H, m), 2.25-2.54 (4H, m), 2.80 (1H, dd, J=14.5, 8 Hz), 3.16 (1H, dd, J=14.5, 7.7 Hz), 3.52 (1H, m), 4.03 (1H, m), 4.28 (1H, dt, J=10, 7 Hz), 4.49 (1H, dd, J=10.7, 10.6 Hz), 4.69 (1H, ddd, J=9.8, 8, 7.7 Hz), 4.74 (1H, m), 6.28 (1H, d, J=10.6 Hz),  
15 6.32 (1H, d, J=9.8 Hz), 6.81 (2x1H, d, J=8.7 Hz), 7.12 (2x1H, d, J=8.7 Hz), 7.24 (1H, d, J=10 Hz), 9.73 (1H, s);

MASS (ES-): m/e 513.

#### Preparation 231

Compound (231) was obtained in a manner similar to Preparation 20 24.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.27-1.97 (10H, m), 1.41 (9x1/6H, s), 1.43 (9x5/6H, s), 2.64 (1H, m), 2.70-3.08 (4H, m), 3.56 (1H, m), 3.71 (3x1/6H, s), 3.73 (3x5/6H, s), 4.06 (1H, m), 4.27 (2H, brt, J=7 Hz), 4.31 (1H, dd, J=8, 4 Hz), 4.68 (1H, m), 4.90 (1H, m), 5.10 (1H, d, J=12 Hz), 5.16 (1H, d, J=12 Hz), 5.18 (1H, d, J=7 Hz), 6.68 (2x1/6H, d, J=8.5 Hz), 6.73-6.92 (2H, m), 6.80 (2x5/6H, d, J=8.5 Hz), 7.08 (2H, d, J=8.5 Hz), 7.12-7.38 (9H, m), 7.42 (2H, dd, J=7.5, 7.5 Hz), 7.55 (1H, dd, J=7.5, 7.5 Hz), 8.03 (2H, d, J=7.5 Hz);

MASS (ES+): m/e 863.

#### Preparation 232

Compound (232) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.18-2.14 (10H, m), 1.41 (3x3H, s), 2.36 (3H, s), 2.68 (1H, m), 2.84-3.10 (4H, m), 3.72 (1H, m), 3.74 (3H, s),  
35 4.06 (1H, m), 4.22-4.36 (3H, m), 4.70 (1H, m), 4.81 (1H, m), 5.29 (1H, brd, J=7.5 Hz), 6.78 (2x1H, d, J=8.5 Hz), 6.92 (1H, br), 7.04 (2x1H,

brd, J=8.5 Hz), 7.14-7.32 (5H, m), 7.42 (2x1H, dd, J=7.5, 7.5 Hz),  
7.48-7.60 (2H, m), 8.02 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES-): m/e 771.

#### Preparation 233

5           Compound (233) was obtained in a manner similar to Preparation  
18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.12-1.98 (10H, m), 2.70-2.90 (2H, m),  
2.91-3.12 (3H, m), 3.65 (3H, s), 4.07-4.34 (4H, m), 4.58 (1H, m), 5.07  
(1H, m), 6.75 (2x1H, d, J=8.5 Hz), 7.13-7.30 (7H, m), 7.40 (2x1H, dd,  
10 J=7.5, 7.5 Hz), 7.52 (1H, dd, J=7.5, 7.5 Hz), 7.98-8.12 (2H, br), 8.02  
(2x1H, d, J=7.5 Hz);

MASS (ES-): m/e 671.

#### Preparation 234

15           Compound (234) was obtained in a manner similar to Preparation  
76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.44 (2H, m), 1.66-1.96 (6H, m), 2.13-2.40  
(2H, m), 2.77 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13, 5 Hz), 3.02-  
3.24 (3H, m), 3.77 (3H, s), 3.94 (1H, m), 4.24-4.35 (2H, m), 4.61 (1H,  
dd, J=8, 2.5 Hz), 4.69 (1H, m), 5.06 (1H, ddd, J=10, 10, 5 Hz), 6.24  
20 (1H, d, J=10 Hz), 6.44 (1H, d, J=10 Hz), 6.81 (2x1H, d, J=8.5 Hz),  
7.09-7.32 (8H, m), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.03  
(2H, dd, J=7.5, 1.5 Hz);

MASS (ES-) m/e 653.

#### Preparation 235

25           Compound (235) was obtained in a manner similar to Preparation  
77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.24-1.91 (8H, m), 2.10-2.40 (2H, m), 2.78  
(1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13.5, 5.5 Hz), 3.02-3.24 (3H,  
m), 3.63 (2H, brt, J=6 Hz), 3.78 (3H, s), 3.94 (1H, m), 4.28 (1H, dt,  
30 J=10, 8 Hz), 4.61 (1H, dd, J=8, 3 Hz), 4.69 (1H, m), 5.06 (1H, ddd,  
J=10, 10, 5.5 Hz), 6.35 (1H, d, J=10 Hz), 6.46 (1H, d, J=10 Hz), 6.82  
(2x1H, d, J=8.5 Hz), 7.09-7.32 (8H, m);

MASS (ES-): m/e 549.

#### Preparation 236

35           Compound (236) was obtained in a manner similar to Preparation  
78. The obtained compound was used in Example 105.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.48-1.90 (4H, m), 2.10-2.50 (4H, m), 2.78 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13.5, 5 Hz), 3.07 (1H, m), 3.16 (1H, dd, J=14, 8.5 Hz), 3.18 (1H, dd, J=13.5, 11 Hz), 3.78 (3H, s), 3.94 (1H, m), 4.28 (1H, dt, J=10.3, 7.3 Hz), 4.62 (1H, dd, J=8, 2.5 Hz), 4.68 (1H, ddd, J=10, 8.5, 7 Hz), 5.06 (1H, ddd, J=11, 10, 5 Hz), 6.32 (1H, d, J=10 Hz), 6.82 (2x1H, d, J=9 Hz), 7.09-7.32 (8H, m), 9.74 (1H, t, J=1 Hz);

MASS (ES-): m/e 547.

Preparation 237

10 Compound (237) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40 (3x3H, s), 1.80 (1H, m), 1.90-2.11 (3H, m), 3.12 (1H, m), 3.73 (1H, m), 4.48 (1H, m), 5.17 (1H, d, J=12 Hz), 5.23 (1H, d, J=12 Hz), 5.43 (1H, d, J=7 Hz), 6.12 (1H, d, J=7 Hz), 7.23-7.45 (10H, m);

MASS (ES+): m/e 439.

Preparation 238

Compound (238) was obtained in a manner similar to Preparation 21.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.72-2.10 (4H, m), 2.71 (1H, m), 3.82 (1H, m), 4.46 (1H, m), 5.12 (1H, dd, J=12.5 Hz), 5.22 (1H, dd, J=12.5 Hz), 5.50 (1H, s), 7.30-7.54 (10H, m), 8.66 (2H, brs);

MASS (ES+): m/e 339.

Preparation 239

25 Compound (239) was obtained in a manner similar to Preparation 22.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.71 (3H, t, J=7.5 Hz), 1.36 (3x3H, brs), 1.42 (3H, s), 1.56-2.10 (6H, m), 3.11 (1H, m), 3.74 (1H, m), 4.49 (1H, m), 5.16 (2H, s), 5.64 (1H, d, J=6.5 Hz), 7.21-7.43 (11H, m), 7.63 (1H, d, J=6.5 Hz);

MASS (ES+): m/e 538.

Preparation 240

Compound (240) was obtained in a manner similar to Preparation 23.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.95 (3H, t, J=7 Hz), 1.60 (3H, s), 1.70-2.19 (6H, m), 3.09 (1H, m), 3.78 (1H, m), 4.48 (1H, m), 5.16 (2H, s),

5.73 (1H, d, J=6.5 Hz), 7.22-7.45 (10H, m), 7.62 (1H, d, J=6.5 Hz),  
8.02 (2H, brs);  
MASS (ES+): m/e 438.

#### Preparation 241

5           Compound (241) was obtained in a manner similar to Preparation 24.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, t, J=7.5 Hz), 1.36-2.42 (12H, m),  
1.41 (3x3H, s), 1.47 (3H, s), 3.11 (1H, m), 3.73 (1H, m), 4.04 (1H,  
m), 4.28 (2H, t, J=6 Hz), 4.50 (1H, m), 5.07 (1H, br), 5.16 (1H, d,  
10 J=12.5 Hz), 5.19 (1H, d, J=12.5 Hz), 5.62 (1H, d, J=6 Hz), 7.03 (1H,  
s), 7.26-7.48 (13H, m), 7.54 (1H, m), 8.01 (2x1H, dd, J=7, 1.5 Hz);  
MASS (ES+): m/e 793 (M+Na).

#### Preparation 242

15           Compound (242) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.68 (3H, brt, J=7 Hz), 1.34-2.21 (12H, m),  
1.42 (3x3H, s), 1.44 (3H, s), 3.12 (1H, m), 3.77 (1H, m), 4.05 (1H,  
m), 4.33 (2H, brt, J=6 Hz), 4.46 (1H, m), 5.14 (1H, br), 5.67 (1H, d,  
J=7 Hz), 6.89 (1H, brs), 7.24-7.47 (7H, m), 7.56 (1H, m), 7.69 (1H,  
20 brd, J=7 Hz), 8.03 (2x1H, dd, J=7.5, 1 Hz);  
MASS (ES-): m/e 679.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.57 (3x7/9H, t, J=7.5 Hz), 0.62 (3x2/9H,  
t, J=7.5 Hz), 1.26-2.08 (12H, m), 1.33 (3H, s), 1.34 (3x3H, s), 3.12  
(1H, m), 3.75 (1H, m), 3.88 (1H, m), 4.19-4.32 (3H, m), 5.58 (1x2/9H,  
25 d, J=7.5 Hz), 5.68 (1x7/9H, d, J=7.5 Hz), 6.94 (1H, d, J=8.5 Hz),  
7.22-7.41 (5H, m), 7.52 (2x1H, dd, J=7.5, 7.5 Hz), 7.66 (1H, m), 7.78  
(1H, s), 7.96 (2x1H, dd, J=7.5, 1.5 Hz).

#### Preparation 243

30           Compound (243) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, t, J=7 Hz), 1.42 (3H, s), 1.54-  
2.16 (12H, m), 3.09 (1H, m), 3.83 (1H, m), 4.26-4.54 (4H, m), 5.77  
(1H, d, J=7 Hz), 7.25-7.42 (7H, m), 7.51 (1H, dd, J=7.5, 7.5 Hz), 7.58  
(1H, br), 7.91 (2H, brs), 8.02 (2x1H, d, J=7.5 Hz), 8.62 (1H, s);  
35 MASS (ES+): m/e 581.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.59 (3H, t, J=7.5 Hz), 1.32-1.92 (12H,

m), 1.37 (3H, s), 3.07 (1H, m), 3.74 (1H, m), 3.88 (1H, m), 1.25 (1H, dd, J=8, 2 Hz), 4.30 (2H, t, J=6 Hz), 5.65 (1H, d, J=7 Hz), 7.25-7.40 (5H, m), 7.52 (1H, dd, J=7.5, 7.5 Hz), 7.66 (1H, m), 7.90 (2H, d, J=7 Hz), 7.98 (2x1H, dd, J=7.5, 1.5 Hz), 8.15 (2H, br), 8.40 (1H, s).

5 Preparation 244

Compound (244) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.90 (3H, t, J=7.3 Hz), 1.36 (3H, s), 1.48 (2H, m), 1.58-2.56 (10H, m), 3.76 (1H, m), 4.04 (1H, m), 4.30 (1H, m),  
10 4.32 (2H, t, J=6.5 Hz), 4.76 (1H, m), 5.99 (1H, s), 6.20 (1H, d, J=10 Hz), 7.17 (1H, d, J=10 Hz), 7.28-7.49 (7H, m), 7.56 (1H, m), 8.04 (2H, m), 8.10 (1H, d, J=10 Hz);

MASS (ES<sup>+</sup>): m/e 563.

Preparation 245

15 Compound (245) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.92 (3H, t, J=7.5 Hz), 1.36 (3H, s), 1.39 (2H, m), 1.52-1.71 (4H, m), 1.79-2.06 (3H, m), 2.10-2.53 (4H, m), 3.65 (1H, dt, J=6, 6 Hz), 3.74 (1H, m), 4.04 (1H, m), 4.27 (1H, dt, J=10, 7.5 Hz),  
20 4.75 (1H, dd, J=8, 2 Hz), 5.97 (1H, s), 6.19 (1H, d, J=10.5 Hz), 7.14 (1H, d, J=10 Hz), 7.28-7.43 (5H, m), 8.08 (1H, d, J=10.5 Hz);

MASS (ES<sup>+</sup>): m/e 459.

Preparation 246

25 Compound (246) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 108.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.92 (3H, t, J=7.4 Hz), 1.26 (3H, s), 1.52-1.74 (3H, m), 1.78-2.06 (3H, m), 2.12-2.54 (6H, m), 3.74 (1H, dt, J=10, 7 Hz), 4.04 (1H, m), 4.28 (1H, dt, J=10.5, 7 Hz), 4.76 (1H, dd, J=8, 2 Hz),  
30 6.05 (1H, s), 6.18 (1H, d, J=10 Hz), 7.18 (1H, d, J=10 Hz), 7.28-7.42 (5H, m), 8.02 (1H, d, J=10 Hz), 9.77 (1H, brs);

MASS (ES<sup>-</sup>): m/e 455.

Preparation 247

35 Compound (247) was obtained in a manner similar to Preparation 20.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60-2.30 (17H, m), 1.41 (9x1/4H, s), 1.44

(9x3/4H, s), 3.42-3.64 (1H, m), 3.84 (1H, m), 4.27 (1x1/4H, m), 4.47 (1x3/4H, m), 4.58 (1H, m), 4.97 (1H, m), 5.13 (1H, d, J=12.5 Hz), 5.13-5.23 (1H, m), 5.19 (1H, d, J=12.5 Hz), 7.28-7.42 (5H, m);  
MASS (ES+): m/e 459.

5 Preparation 248

Compound (248) was obtained in a manner similar to Preparation 21.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.68-1.34 (5H, m), 1.38-1.76 (7H, m), 1.82-2.06 (4H, m), 2.18 (1H, m), 3.42 (1H, m), 3.80 (1H, m), 4.25 (1H, brt, J=6 Hz), 4.39 (1H, dd, J=8.5, 2.5 Hz), 5.10 (1H, d, J=12.5 Hz), 5.18 (1H, d, J=12.5 Hz), 7.13-7.44 (5H, m), 8.20 (2H, brs);  
MASS (ES+): m/e 359.

Preparation 249

15 Compound (249) was obtained in a manner similar to Preparation 22.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.68 (3x2/3H, brt, J=7 Hz), 0.77-2.30 (19H, m), 0.84 (3x1/3H, brt, J=7 Hz), 1.24 (3x1/3H, s), 1.27 (3x2/3H, s), 1.33 (9x1/3H, s), 1.36 (9x2/3H, s), 3.50 (1H, m), 3.69 (1H, m), 4.31 (1H, dd, J=8, 3 Hz), 4.42 (1x1/3H, m), 4.69 (1x2/3H, m), 5.03 (1H, d, J=12.5 Hz), 5.10 (1H, d, J=12.5 Hz), 6.54 (1x1/3H, br), 6.67 (1x2/3H, br), 7.31-7.42 (5H, m), 7.44 (1x1/3H, d, J=8 Hz), 7.70 (1x2/3H, d, J=8 Hz);  
MASS (ES+): m/e 558.

Preparation 250

25 Compound (250) was obtained in a manner similar to Preparation 23.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.74 (3x1/4H, t, J=7.5 Hz), 0.78 (3x3/4H, t, J=7.5 Hz), 0.82-2.28 (19H, m), 1.44 (3x1/4H, s), 1.47 (3x3/4H, s), 3.56 (1H, m), 3.77 (1H, m), 4.33 (1H, dd, J=8.5, 3 Hz), 4.78 (1x3/4H, m), 5.01 (1H, d, J=12.5 Hz), 5.04 (1x1/4H, m), 5.16 (1H, d, J=12.5 Hz), 7.29-7.42 (5H, m), 8.15 (2H, brs), 8.46 (1x3/4H, d, J=8.5 Hz), 8.62 (1x1/4H, d, J=8.5 Hz);  
MASS (ES+): m/e 458.

Preparation 251

35 Compound (251) was obtained in a manner similar to Preparation 24.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.57 (3H, t, J=7.3 Hz), 0.70-2.30 (25H, m), 1.34 (3H, s), 1.36 (3x3H, s), 3.52 (1H, m), 3.66-3.84 (2H, m), 4.24 (2H, t, J=6.5 Hz), 4.31 (1H, dd, J=9, 3 Hz), 4.76 (1H, m), 5.01 (1H, d, J=12.5 Hz), 5.12 (1H, d, J=12.5 Hz), 7.14 (1H, m), 7.29-7.42 (5H, m), 7.51 (2H, m), 7.65 (1H, m), 7.70 (1H, s), 7.80 (1H, d, J=6.5 Hz), 7.95 (2x1H, d, J=7 Hz);

MASS (ES+): m/e 791.

#### Preparation 252

Compound (252) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.76-2.36 (25H, m), 0.80 (3H, t, J=7.5 Hz), 1.43 (3x3H, s), 1.48 (3H, s), 3.50 (1H, m), 3.93 (1H, m), 4.02 (1H, m), 4.33 (2H, t, J=6.5 Hz), 4.59 (1H, m), 4.86 (1H, m), 5.23 (1H, m), 6.91 (1H, s), 7.16 (1H, d, J=8.5 Hz), 7.43 (2x1H, dd, J=8, 8 Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=8, 1.5 Hz);

MASS (ES-): m/e 699.

#### Preparation 253

Compound (253) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.67 (3x1/2H, t, J=7.5 Hz), 0.68 (3x1/2H, t, J=7.5 Hz), 0.72-2.32 (25H, m), 1.40 (3x1/2H, s), 1.41 (3x1/2H, s), 3.33 (1H, m), 3.48 (1x1/2H, m), 3.71 (1x1/2H, m), 3.96 (1H, m), 4.18 (1x1/2H, dd, J=8.5, 2.5 Hz), 4.27 (2x1/2H, t, J=6.2 Hz), 4.29 (2x1/2H, t, J=6.2 Hz), 4.42 (1x1/2H, m), 4.75 (1x1/2H, m), 4.81 (1x1/2H, d, J=8, 2 Hz), 7.53 (2x1/2H, dd, J=7.5, 7.5 Hz), 7.67 (1H, dd, J=7.5, 7.5 Hz), 7.75 (1x1/2H, d, J=8.5 Hz), 7.88 (1x1/2H, d, J=8.5 Hz), 7.96 (2x1H, d, J=7.5 Hz), 8.05 (2H, br), 8.14 (1x1/2H, s), 8.16 (1x1/2H, s);

MASS (ES+): m/e 601.

#### Preparation 254

Compound (254) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7 Hz), 0.96 (2H, m), 1.08-1.26 (4H, m), 1.28 (3H, s), 1.45 (2H, m), 1.55-1.98 (13H, m), 2.07-2.42 (4H, m), 3.52 (1H, m), 3.96 (1H, m), 4.24 (1H, ddd, J=10, 8, 8 Hz), 4.31 (2H, t, J=6 Hz), 4.74 (1H, m), 5.00 (1H, ddd, J=10, 8, 8

Hz), 5.83 (1H, s), 7.14 (1H, d, J=10 Hz), 7.34 (1H, d, J=10 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dd, J=7.5, 7.5 Hz), 8.03 (2x1H, d, J=7.5 Hz);

MASS (ES-): m/e 581.

5 Preparation 255

Compound (255) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.3 Hz), 0.96 (2H, m), 1.08-1.51 (6H, m), 1.53-2.00 (11H, m), 2.09-2.43 (4H, m), 3.51 (1H, ddd, J=10, 7.5, 7 Hz), 3.65 (2H, brt, J=5 Hz), 3.96 (1H, m), 4.23 (1H, ddd, J=10, 8, 7 Hz), 4.74 (1H, dd, J=8, 2 Hz), 4.99 (1H, ddd, J=10, 8, 8 Hz), 6.01 (1H, s), 7.16 (1H, d, J=10 Hz), 7.35 (1H, d, J=10 Hz);

MASS (ES-): m/e 477.

Preparation 256

15 Compound (256) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 111, 114.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.3 Hz), 0.96 (2H, m), 1.08-1.35 (4H, m), 1.30 (3H, s), 1.50-2.02 (13H, m), 2.10-2.44 (4H, m), 2.49 (2H, m), 3.52 (1H, dt, J=10, 7.3 Hz), 3.96 (1H, m), 4.23 (1H, ddd, J=10, 7.5, 7 Hz), 4.74 (1H, dd, J=8, 2 Hz), 4.99 (1H, dt, J=10, 7.5 Hz), 5.89 (1H, s), 7.16 (1H, d, J=10 Hz), 7.29 (1H, d, J=10 Hz), 9.76 (1H, t, J=1 Hz);

MASS (ES-): m/e 475.

Preparation 257

25 Compound (257) was obtained in a manner similar to Preparation 22.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.18-2.18 (14H, m), 1.41 (9x3/4H, s), 1.48 (9x1/4H, s), 2.64 (1H, m), 2.88 (1H, m), 3.03 (1x3/4H, m), 3.15 (1x1/4H, m), 3.50 (1x3/4H, m), 3.58 (1x1/4H, m), 4.17 (1H, dd, J=8, 3.5 Hz), 4.68-5.14 (3H, m), 6.86-7.44 (12H, m);

MASS (ES+): m/e 578.

Preparation 258

Compound (258) was obtained in a manner similar to Preparation 23.

35 <sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.82-2.14 (14H, m), 1.35 (9x5/6H, s), 1.45 (9x5/6H, s), 2.83 (1H, dd, J=13, 5 Hz), 2.92 (1H, dd, J=13, 6.5

Hz), 3.17 (1H, m), 3.40 (1x1/6H, m), 3.53 (1x5/6H, m), 4.06 (1x5/6H, dd, J=8.5, 3.5 Hz), 4.47 (1x1/6H, m), 4.73 (1x5/6H, m), 4.84 (1x1/6H, m), 7.11-7.30 (5H, m), 8.30 (1H, d, J=8.5 Hz);

MASS (ES+): m/e 444.

5 Preparation 259

Compound (259) was obtained in a manner similar to Preparation 24.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.12-2.28 (20H, m), 1.42 (3x3H, s), 1.44 (3x3H, s), 2.69 (1H, m), 2.92 (1H, dd, J=13.5, 9.5 Hz), 3.03 (1H, dd, J=13.5, 5 Hz), 3.51 (1H, m), 3.93-4.20 (2H, m), 4.33 (2H, brt, J=6 Hz), 4.88 (1H, m), 5.17 (1H, br), 6.51 (1H, brs), 7.12-7.32 (6H, m), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dd, J=7.5, 7.5 Hz), 8.03 (2x1H, d, J=7.5 Hz);

MASS (ES-): m/e 775.

15 Preparation 260

Compound (260) was obtained in a manner similar to Preparation 57.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.06-2.10 (19H, m), 2.32 (1H, m), 2.87-3.07 (3H, m), 3.74 (1H, m), 4.08-4.42 (4H, m), 4.74 (1H, m), 7.14-7.32 (6H, m), 7.38-7.62 (4H, m), 7.77 (2H, br), 8.02 (2x1H, d, J=8 Hz);

MASS (ES+): m/e 620.

Preparation 261

Compound (261) was obtained in a manner similar to Preparation 76.

25 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.26-1.96 (16H, m), 2.04 (1H, m), 2.17 (1H, m), 2.30 (1H, m), 2.62 (1H, m), 2.95 (1H, dd, J=13.6 Hz), 3.21 (1H, m), 3.25 (1H, dd, J=13, 10 Hz), 3.92 (1H, m), 4.25 (1H, ddd, J=10, 8, 7.5 Hz), 4.32 (2H, t, J=6.5 Hz), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.70 (1H, s), 7.15-7.32 (6H, m), 7.38 (1H, d, J=10 Hz), 30 7.44 (2H, m), 7.56 (1H, m), 8.03 (2H, m);

MASS (ES-): m/e 601.

Preparation 262

Compound (262) was obtained in a manner similar to Preparation 77.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.22-1.93 (16H, m), 2.04 (1H, m), 2.16 (1H, m), 2.30 (1H, m), 2.63 (1H, m), 2.95 (1H, dd, J=13.5, 6 Hz), 3.20 (1H,

m), 3.26 (1H, dd, J=13.5, 10 Hz), 3.66 (2H, t, J=6.5 Hz), 3.92 (1H, m), 4.24 (1H, ddd, J=10, 8, 8 Hz), 4.64 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.84 (1H, s), 7.15-7.32 (6H, m), 7.38 (1H, d, J=10 Hz);  
MASS (ES-): m/e 497.

5 Preparation 263

Compound (263) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 117, 120.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.20-1.93 (14H, m), 1.98-2.67 (6H, m), 2.95 (1H, dd, J=14, 5 Hz), 3.20 (1H, m), 3.24 (1H, dd, J=14, 10 Hz), 3.92 (1H, m), 4.24 (1H, m), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 5, 5 Hz), 5.76 (1H, s), 7.15-7.40 (7H, m), 9.77 (1H, t, J=1 Hz);  
MASS (ES-): m/e 495.

Preparation 264

Compound (264) was obtained in a manner similar to Preparation 77. The obtained compound was used in Examples 117, 120.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.24-1.90 (14H, m), 1.96-2.25 (2H, m), 2.32 (1H, m), 2.50 (2H, m), 2.60 (1H, m), 2.95 (1H, dd, J=13.5, 6 Hz), 3.20 (1H, m), 3.24 (1H, dd, J=13.5, 10 Hz), 3.93 (1H, m), 4.24 (1H, m), 4.66 (1H, dd, J=8, 2.5 Hz), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.76 (1H, s), 7.16-7.34 (6H, m), 7.34 (1H, d, J=10 Hz), 9.77 (1H, t, J=1 Hz);  
MASS (ES-): m/e 495.

Preparation 265

Compound (265) was obtained in a manner similar to Preparation 21.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.52 (1H, m), 1.66-2.01 (3H, m), 2.71 (1H, m), 2.96 (1H, dd, J=13.5, 8 Hz), 3.14 (1H, dd, J=13.5, 6 Hz), 3.55 (1H, m), 4.26 (1H, dd, J=8.5, 3.5 Hz), 4.41 (1H, br), 5.08 (1H, d, J=12.5 Hz), 5.19 (1H, d, J=12.5 Hz), 7.16-7.46 (10H, m), 8.41 (2H, brs);

MASS (ES+): m/e 353.

Preparation 266

Compound (266) was obtained in a manner similar to Preparation 22.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.75-2.00 (17H, m), 1.41 (9x1/4H, s), 1.46 (9x3/4H, s), 2.63 (1H, m), 2.93 (1H, dd, J=13.5, 9.5 Hz), 3.06 (1H, dd, J=13.5, 6 Hz), 3.50 (1x3/4H, m), 3.60 (1x1/4H, m), 4.04 (1x1/4H,

m), 4.19 (1x3/4H, m), 4.36 (1H, dd, J=8, 4 Hz), 4.75 (1H br), 4.94 (1H, ddd, J=9.5, 7, 6 Hz), 5.10 (1H, d, J=12.5 Hz), 5.19 (1H, d, J=12.5 Hz), 6.82 (1x3/4H, brd, J=7 Hz), 7.04 (1x1/4H, brd, J=7 Hz), 7.14-7.41 (10H, m);

5 MASS (ES-): m/e 604.

Preparation 267

Compound (267) was obtained in a manner similar to Preparation 23.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.68-2.32 (17H, m), 2.80 (1/2H, m), 2.95-3.16 (2H, m), 3.50-3.80 (1+1/2H, m), 4.26-4.46 (1x1/2H, m), 4.62 (1x1/2H, m), 4.86 (1x1/2H, m), 5.10-5.24 (2H, m), 5.36 (1/2H, m), 7.12-7.40 (10H, m), 8.16 (1H, br), 8.36-8.54 (1x1/2H, m), 8.75 (1x1/2H, br);

MASS (ES+): m/e 506.

15 Preparation 268

Compound (268) was obtained in a manner similar to Preparation 24.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.69-2.06 (23H, m), 1.42 (9x1/7H, s), 1.43 (9x6/7H, s), 2.72 (1H, m), 2.92-3.08 (2H, m), 3.57 (1H, m), 4.12 (1H, m), 4.25-4.40 (3H, m), 4.52 (1H, m), 4.93 (1H, m), 5.10 (1H, d, J=12.5 Hz), 5.17 (1H, d, J=12.5 Hz), 5.20 (1H, br), 6.39 (1x1/7H, d, J=8.5 Hz), 6.58 (1x6/7H, d, J=8.5 Hz), 6.86 (1H, brd, J=7 Hz), 7.15-7.39 (10H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

25 MASS (ES-): m/e 837.

Preparation 269

Compound (269) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.64-2.12 (23H, m), 1.45 (3x3H, s), 2.67 (1H, m), 2.95-3.11 (2H, m), 3.71 (1H, m), 4.08 (1H, m), 4.26-4.64 (4H, m), 4.74 (1H, m), 5.89 (1H, br), 6.95 (1H, br), 7.13-7.34 (5H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dd, J=7.5, 7.5 Hz), 7.73 (1H, br), 8.04 (2x1H, d, J=7.5 Hz);

MASS (ES-): m/e 747.

35 Preparation 270

Compound (270) was obtained in a manner similar to Preparation

57.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70-0.90 (2H, m), 1.94-1.30 (6H, m), 1.36-1.67 (7H, m), 1.70-2.18 (8H, m), 2.87-3.01 (2H, m), 3.11 (1H, m), 3.72 (1H, m), 3.96 (1H, m), 4.10 (1H, m), 4.33 (2H, t, J=6 Hz), 4.48-4.62 (2H, m), 7.18-7.34 (5H, m), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, dd, J=7.5, 7.5 Hz), 7.90 (1H, d, J=8 Hz), 8.04 (2x1H, d, J=7.5 Hz), 8.34 (2H, br), 9.07 (1H, d, J=7 Hz);

MASS (ES+): m/e 649.

Preparation 271

10 Compound (271) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.91 (2H, m), 1.06-1.34 (5H, m), 1.36-1.99 (14H, m), 2.18 (1H, m), 2.31 (1H, m), 2.94 (1H, dd, J=13, 5 Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13, 10 Hz), 3.93 (1H, m), 4.31 (1H, t, J=6.5 Hz), 4.31 (1H, m), 4.52 (1H, dt, J=10, 7.5 Hz), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10, 5 Hz), 6.06 (1H, d, J=10 Hz), 6.49 (1H, d, J=10 Hz), 7.15-7.32 (6H, m), 7.40-7.47 (2H, m), 7.52-7.59 (1H, m), 8.00-8.06 (2H, m);

MASS (ES-) m/e 629.

20 Preparation 272

Compound (272) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.92 (2H, m), 1.08-1.92 (19H, m), 2.18 (1H, m), 2.31 (1H, m), 2.94 (1H, dd, J=13.5, 5.5 Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13.5, 10 Hz), 3.66 (1H, dt, J=6, 5 Hz), 3.94 (1H, m), 4.29 (1H, dt, J=10, 7 Hz), 4.52 (1H, dt, J=10, 7.5 Hz), 4.63 (1H, m), 5.09 (1H, ddd, J=10, 10, 5.5 Hz), 6.15 (1H, d, J=10 Hz), 6.51 (1H, d, J=10 Hz), 7.14-7.33 (6H, m);

MASS (ES-): m/e 525.

30 Preparation 273

Compound (273) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 123, 126, 129.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.90 (2H, m), 1.10-1.32 (4H, m), 1.37-1.95 (13H, m), 2.11-2.55 (4H, m), 2.94 (1H, dd, J=13, 5 Hz), 3.09 (1H, m), 3.21 (1H, dd, J=13, 10 Hz), 3.94 (1H, m), 4.31 (1H, m), 4.52 (1H, dt, J=10, 7 Hz), 4.63 (1H, m), 5.08 (1H, ddd, J=10, 10, 5 Hz), 6.13 (0.6H,

d, J=10 Hz), 6.32 (0.4H, d, J=10 Hz), 6.50 (0.6H, d, J=10 Hz), 6.61 (0.4H, d, J=10 Hz), 7.17-7.34 (6H, m), 9.76 (1H, t);

MASS (ES+): m/e 525.

Preparation 274

5 Compound (274) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.44 (9x1/5H, s), 1.46 (9x4/5H, s), 1.78-2.24 (6H, m), 2.69 (2H, t, J=8 Hz), 3.31 (1x4/5H, m), 3.60 (1x1/5H, m), 3.70 (1x4/5H, m), 4.25 (1x1/5H, m), 4.42 (1x4/5H, dd, J=8, 3 Hz),  
10 4.54 (1x4/5H, m), 4.70 (1x1/5H, m), 4.93 (1x1/5H, m), 5.00 (1x1/5H, d, J=12.5 Hz), 5.07 (1x1/5H, d, J=12.5 Hz), 5.12 (1x4/5H, d, J=12.5 Hz), 5.20 (1x4/5H, d, J=12.5 Hz), 5.40 (1H, brd, J=8 Hz), 7.10-7.41 (10H, m);

MASS (ES+): m/e 467.

15 Preparation 275

Compound (275) was obtained in a manner similar to Preparation 21.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.80-2.10 (6H, m), 2.70 (2H, m), 3.40 (1H, m), 3.65 (1H, m), 4.25 (1H, m), 4.35 (1H, m), 5.10 (1H, d, J=12 Hz),  
20 5.19 (1H, d, J=12 Hz), 7.05-7.44 (10H, m), 8.42 (2H, brs);

MASS (ES+): m/e 367.

Preparation 276

Compound (276) was obtained in a manner similar to Preparation 22.

25 <sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.71 (3H, t, J=7.3 Hz), 1.28 (3x1/4H, s), 1.29 (3x3/4H, s), 1.34 (9x1/4H, s), 1.36 (9x3/4H, s), 1.70-2.62 (10H, m), 3.24-3.44 (3H, m), 3.58 (1H, m), 4.30 (1H, dd, J=9, 3.5 Hz), 4.60 (1H, m), 5.04 (1H, d, J=13 Hz), 5.10 (1H, d, J=13 Hz), 6.63 (1x1/4H, brs), 6.80 (1x3/4H, brs), 7.05-7.41 (10H, m), 7.58 (1x3/4H, d, J=9 Hz),  
30 7.92 (1x1/4H, d, J=9 Hz);

MASS (ES+): m/e 566.

Preparation 277

Compound (277) was obtained in a manner similar to Preparation 23.

35 <sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.80 (3H, t, J=7 Hz), 1.52 (3x1/5H, s), 1.54 (3x4/5H, s), 1.66-2.75 (8H, m), 3.39 (1H, m), 3.60 (1H, m), 4.33

(1H, dd, J=9, 3 Hz), 4.63 (1H, m), 5.00 (1x4/5H, d, J=13 Hz), 5.06 (1x1/5H, dd, J=13 Hz), 5.12 (1x1/5H, d, J=13 Hz), 5.16 (1x4/5H, d, J=13 Hz), 7.08 (1H, brd, J=7 Hz), 7.16-7.42 (9H, m), 8.16 (2x4/5H, brs), 8.20 (2x1/5H, brs), 8.57 (1x4/5H, d, J=8.5 Hz), 8.74 (1x1/5H, d, J=8.5 Hz);

MASS (ES+): m/e 466.

Preparation 278

Compound (278) was obtained in a manner similar to Preparation 24.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.76 (3H, t, J=7 Hz), 1.43 (3x3H, s), 1.45-2.58 (14H, m), 1.53 (3H, s), 2.65 (2H, t, J=8 Hz), 3.32 (1H, m), 3.68 (1H, m), 4.08 (1H, m), 4.31 (2H, t, J=6 Hz), 4.44 (1H, dd, J=8, 2.5 Hz), 4.82 (1H, m), 5.12 (1H, m), 5.13 (2H, s), 6.78 (1H, brd, J=8 Hz), 7.01 (1H, s), 7.09-7.38 (10H, m), 7.39-7.47 (2H, m), 7.55 (1H, m), 8.00-8.06 (2H, m);

MASS (ES+): m/e 799.

Preparation 279

Compound (279) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.5 Hz), 1.42 (3x3H, s), 1.44-2.30 (14H, m), 1.46 (3H, s), 2.66 (2H, t, J=7 Hz), 3.26 (1H, m), 3.74 (1H, m), 4.02 (1H, m), 4.32 (2H, brt, J=6 Hz), 4.42 (1H, m), 4.77 (1H, m), 6.89 (1H, s), 7.11-7.31 (7H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES-): m/e 707.

Preparation 280

Compound (280) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.5 Hz), 1.37 (3H, s), 1.58 (2H, m), 1.72-2.24 (12H, m), 2.60 (1H, m), 2.72 (1H, m), 3.19 (1H, m), 3.63 (1H, m), 4.09 (1H, m), 4.23-4.38 (3H, m), 4.61 (1H, m), 7.12-7.32 (6H, m), 7.42 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 7.60 (1H, brd, J=9 Hz), 7.78 (2H, br), 8.01 (2x1H, d, J=7.5 Hz);

MASS (ES+): m/e 609.

Preparation 281

Compound (281) was obtained in a manner similar to Preparation

76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7 Hz), 1.28 (3H, s), 1.45 (2H, m), 1.61-1.97 (6H, m), 1.98-2.43 (6H, m), 2.64 (2H, m), 3.32 (1H, m), 3.75 (1H, m), 4.24 (1H, dt, J=10, 7.5 Hz), 4.31 (1H, t, J=6.5 Hz),  
5 4.72 (1H, m), 4.84 (1H, dt, J=10, 7.5 Hz), 5.81 (1H, s), 7.11 (1H, d, J=10 Hz), 7.14-7.23 (3H, m), 7.24-7.32 (2H, m), 7.38-7.48 (3H, m), 7.52-7.60 (2H, m), 8.00-8.06 (2H, m);

MASS (ES-): m/e 589.

Preparation 282

10 Compound (282) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7 Hz), 1.28 (3H, s), 1.30-1.70 (5H, m), 1.75-1.92 (3H, m), 2.00-2.42 (6H, m), 2.64 (2H, m), 3.32 (1H, m), 3.65 (2H, brt, J=6 Hz), 3.74 (1H, m), 4.22 (1H, dt, J=10, 7.5  
15 Hz), 4.72 (1H, m), 4.84 (1H, dt, J=10, 7.5 Hz), 5.91 (1H, s), 7.10 (1H, d, J=10 Hz), 7.14-7.23 (3H, m), 7.24-7.33 (2H, m), 7.41 (1H, d, J=10 Hz);

MASS (ES-): m/e 485.

Preparation 283

20 Compound (283) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 132, 135.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.5 Hz), 1.29 (3H, s), 1.58-1.73 (2H, m), 1.76-1.91 (3H, m), 1.98-2.24 (5H, m), 2.26-2.42 (3H, m), 2.50 (2H, m), 2.64 (2H, m), 3.32 (1H, m), 3.75 (1H, m), 4.23 (1H, m),  
25 4.72 (1H, m), 4.84 (1H, ddd, J=10, 8, 7 Hz), 5.85 (1H, s), 7.12 (1H, d, J=10.5 Hz), 7.14-7.32 (5H, m), 7.36 (1H, d, J=10 Hz), 9.77 (1H, t, J=1 Hz);

MASS (ES-): m/e 483.

Preparation 284

30 Compound (284) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.49 (9H, s), 1.51-1.63 (1H, m), 1.74-2.01 (3H, m), 2.62-2.80 (1H, m), 2.90 (1H, dd, J=12.5, 9.6 Hz), 3.01 (1H, dd, J=12.5, 5.6 Hz), 3.48-3.66 (1H, m), 4.27 (1H, t, J=7.0 Hz), 4.35  
35 (1H, dd, J=8.0, 3.7 Hz), 4.55 (2H, d, J=7.0 Hz), 4.56-4.67 (1H, m), 5.11 (1H, d, J=12.4 Hz), 5.21 (1H, d, J=12.4 Hz), 5.37 (1H, d, J=8.5

Hz), 6.62 (1H, brs), 7.07-7.49 (13H, m), 7.62 (2H, d, J=7.3 Hz), 7.79 (2H, d, J=7.8 Hz);

MASS (ES+): m/e 690.49 (M+1).

#### Preparation 285

5           Compound (285) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.3 Hz), 1.39 (1.5H, s), 1.40 (1.5H, s), 1.43 (9H, s), 1.49-1.65 (2H, m), 1.71-2.07 (4H, m), 2.69-2.85 (1H, m), 2.91 (1H, dd, J=12.9, 9.2 Hz), 3.01 (1H, dd, J=12.9, 5.4 Hz), 3.49-3.62 (1H, m), 4.27 (1H, t, J=6.6 Hz), 4.37 (1H, dd, J=7.8, 3.4 Hz), 4.54 (2H, t, J=6.6 Hz), 4.85-4.98 (1H, m), 5.01-5.20 (3H, m), 6.52-6.67 (1H, m), 6.84 (1H, d, J=8.1 Hz), 7.10-7.19 (2H, m), 7.20-7.38 (9H, m), 7.42 (2H, t, J=7.3 Hz), 7.61 (2H, t, J=7.4 Hz), 7.79 (2H, t, J=7.4 Hz);

15   MASS (ES+): m/e 789.65 (M+1).

#### Preparation 286

Compound (286) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, t, J=7.3 Hz), 1.43 (3H, s), 1.44 (9H, s), 1.45-1.98 (9H, m), 2.15-2.36 (1H, m), 2.74-3.03 (3H, m), 3.52-3.66 (1H, m), 4.20-4.34 (3H, m), 4.39 (1H, dd, J=7.8, 3.5 Hz), 4.52 (2H, t, J=6.6 Hz), 4.85-4.99 (1H, m), 5.01-5.21 (3H, m), 6.61-6.84 (2H, m), 6.98 (1H, s), 7.11 (2H, d, J=8.4 Hz), 7.20-7.36 (1H, m), 7.41 (2H, t, J=7.7 Hz), 7.50-7.58 (1H, m), 7.61 (2H, d, J=7.3 Hz), 7.78 (2H, d, J=7.3 Hz), 8.03 (2H, d, J=6.9 Hz).

#### Preparation 287

Compound (287) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.76 (3H, t, J=7.3 Hz), 1.37-3.01 (15H, m), 1.44 (12H, s), 3.61-3.75 (1H, m), 3.94-4.08 (1H, m), 4.22-4.40 (4H, m), 4.54 (2H, brd, J=6.6 Hz), 4.83-4.98 (1H, m), 5.24 (1H, brs), 6.60 (0.4H, brd, J=8.4 Hz), 6.67 (1H, brs), 6.84 (1H, brs), 6.98 (0.6H, brd, J=8.1 Hz), 7.14 (2H, brd, J=8.1 Hz), 7.21-7.47 (6H, m), 7.48-7.66 (3H, m), 7.71-7.82 (2H, m), 7.99-8.08 (2H, m);

35   MASS (ES+): m/e 932.42 (M+1).

#### Preparation 288

Compound (288) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.71 (3H, brs), 1.38 (3H, brs), 1.47-2.22 (12H, m), 2.74-3.19 (3H, m), 3.56-3.81 (1H, m), 4.08-4.51 (6H, m),  
5 4.82-5.04 (1H, m), 7.02-7.16 (2H, m), 7.17-7.43 (9H, m), 7.44-7.67 (4H, m), 7.69-7.81 (2H, m), 7.91-8.05 (2H, m), 8.11-8.35 (2H, m), 8.37-8.62 (1H, m);  
MASS (ES+): m/e 832.64 (M+1).

Preparation 289

10 Compound (289) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.35-2.02 (8H, m), 2.06-2.24 (2H, m), 2.25-2.41 (2H, m), 2.91 (1H, dd, J=13.6, 6.2 Hz), 3.08-3.32 (2H, m), 3.79-3.92 (1H, m), 4.18-4.30 (2H, m),  
15 4.31 (2H, t, J=6.3 Hz), 4.54 (2H, d, J=6.6 Hz), 4.66 (1H, brd, J=7.0 Hz), 5.14 (1H, dt, J=10.2, 6.3 Hz), 5.90 (1H, s), 6.63 (1H, brs), 7.13 (1H, d, J=10.6 Hz), 7.16 (2H, d, J=8.8 Hz), 7.23-7.37 (4H, m), 7.38-7.48 (4H, m), 7.51-7.65 (4H, m), 7.78 (2H, d, J=7.3 Hz), 8.00-8.07 (2H, m);  
20 MASS (ES+): m/e 813.89 (M).

Preparation 290

Compound (290) was obtained in a manner similar to Preparation 21.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.52 (1H, m), 1.66-1.86 (2H, m), 1.94 (1H, m),  
25 2.72 (1H, m), 2.97 (1H, dd, J=13.5, 8.5 Hz), 3.14 (1H, dd, J=13.5, 6 Hz), 3.56 (1H, m), 4.28 (1H, dd, J=9, 3.5 Hz), 4.41 (1H, brdd, J=8.5, 6 Hz), 5.08 (1H, d, J=12.5 Hz), 5.19 (1H, d, J=12.5 Hz), 7.20-7.43 (10H, m), 8.40 (2H, brs);  
MASS (ES+): m/e 353.

30 Preparation 291

Compound (291) was obtained in a manner similar to Preparation 22.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40 (3x3H, s), 1.47 (1H, m), 1.58-1.94 (3H, m), 2.56 (1H, m), 2.77 (1H, dd, J=13, 10 Hz), 2.83-3.08 (3H, m),  
35 3.48 (1H, m), 3.76 (3H, s), 4.32 (1H, dd, J=8, 4 Hz), 4.84-5.02 (2H, m), 5.10 (1H, d, J=12.5 Hz), 5.17 (1H, d, J=12.5 Hz), 6.67 (1H, d, J=8

Hz), 6.83 (2x1H, d, J=8 Hz), 6.98-7.40 (11H, m), 7.09 (2x1H, d, J=8 Hz);

MASS (ES+): m/e 630.

#### Preparation 292

5 Compound (292) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.70-2.30 (4H, m), 2.41-2.98 (4H, m), 3.26-3.76 (2H, m), 3.70 (3x1/5H, s), 3.71 (3x4/5H, s), 3.83-4.01 (2H, m), 4.32 (1x4/5H, dd, J=8, 3 Hz), 4.44 (1x1/5H, m), 4.88 (1x4/5H, m),  
10 5.06 (1x1/5H, m), 5.10 (1x4/5H, d, J=12.5 Hz), 5.14 (1x4/5H, d, J=12.5 Hz), 5.21 (1x1/5H, d, J=12.5 Hz), 5.31 (1x1/5H, d, J=12.5 Hz), 6.67-6.78 (4x1/5H, m), 6.84 (2x4/5H, d, J=9 Hz), 7.02 (2x4/5H, d, J=9 Hz), 7.08-7.44 (10H, m), 8.07 (2H, br), 9.00 (1x4/5H, d, J=8 Hz), 9.26 (1x1/5H, d, J=8 Hz);

15 MASS (ES+): m/e 530.

#### Preparation 293

Compound (293) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.36-1.56 (2H, m), 1.62-1.98 (6H, m), 2.06-2.40 (4H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.16 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.84 (1H, m), 4.24 (1H, dt, J=10, 7.5 Hz), 4.31 (2H, t, J=6.5 Hz), 4.68 (1H, dd, J=8, 2.5 Hz), 5.12 (1H, ddd, J=10, 9.5, 6 Hz), 5.46 (2H, s), 5.90 (1H, s), 6.73 (2x1H, d, J=8.3 Hz), 7.08 (2x1H, d, J=8.3 Hz), 7.14 (1H, d, J=10 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.52-7.60 (2H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES+): m/e 593.38.

#### Preparation 294

The Compound (293) was dissolved in dichloromethane (30 ml),  
30 ethylisopropylamine (1.76 ml) was added to the mixture. To the mixture was added N-phenylbis(trifluoromethanesulfonimide) (manufactured by Tokyo Kasei Kogyo Co., Ltd., 1.27 g), and the mixture was stirred under ambient temperature overnight. The solvent was removed by evaporation. The residue was dissolved in ethyl acetate,  
35 washed with 5% aqueous potassium hydrogensulfate (x 2), saturated aqueous sodium bicarbonate solution and saturated brine, dried over

sodium sulfate and evaporated. The residue was purified by flush chromatography (Silica gel 60N, Spherical, 45 g, eluting with ethyl acetate/hexane=1/1 then 2/1) to give the objective Compound (294) as a white foam.

5  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.79 (3H, t,  $J=7.5$  Hz), 1.27 (3H, s), 1.38-1.54 (2H, m), 1.66-1.98 (6H, m), 2.06-2.40 (4H, m), 3.02 (1H, dd,  $J=13.5$ , 6.5 Hz), 3.25 (1H, dd,  $J=13.5$ , 9.5 Hz), 3.28 (1H, m), 3.84 (1H, m), 4.25 (1H, dt,  $J=10$ , 7.5 Hz), 4.32 (2x1H, t,  $J=6.5$  Hz), 4.69 (1H, dd,  $J=8$ , 2 Hz), 5.16 (1H, ddd,  $J=10.3$ , 9.5, 6.5 Hz), 5.92 (1H, s),  
10 7.05 (1H, d,  $J=10$  Hz), 7.19 (2x1H, d,  $J=8.7$  Hz), 7.32 (2x1H, d,  $J=8.7$  Hz), 7.44 (2x1H, dd,  $J=7.5$ , 7.5 Hz), 7.56 (1H, m), 8.03 (2x1H, dd,  $J=7.5$ , 1.5 Hz);

MASS (ES<sup>+</sup>): m/e 725.42.

#### Preparation 295

15 To a solution of the Compound (294) (1.4 g) in N,N-dimethylformamide (28 ml) was added lithium chloride (573 mg) and dichlorobis(trichlorophosphine)palladium (II) (67.8 mg), and the mixture was degassed with ultrasonic for 2 min. After purging the air from the reaction vessel with nitrogen, the mixture was stirred at  
20 100°C overnight. The reaction mixture was cooled to ambient temperature, and an aqueous potassium fluoride (2 g/10 ml) was added and the mixture was stirred for 30 min. The reaction mixture was washed with ethyl acetate and the insoluble matter in the mixture was filtered off. The mixture was purified by silica gel column  
25 chromatography (eluting with hexane/ethyl acetate=1/4, ethyl acetate, then hexane/ethyl acetate=9/1) to give the objective Compound (295).  
 $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=7.3$  Hz), 1.11-2.00 (8H, m), 1.28 (3H, s), 2.07-2.24 (2H, m), 2.24-2.43 (2H, m), 2.97-3.07 (1H, m), 3.20-3.37 (2H, m), 3.81-3.94 (1H, m), 4.18-4.30 (1H, m), 4.32 (2H, t,  $J=6.3$  Hz), 4.62-4.70 (1H, m), 5.16-5.28 (1H, m), 5.86 (1H, s), 7.14 (1H, d,  $J=9.9$  Hz), 7.19-7.31 (1H, m), 7.35 (2H, d,  $J=8.4$  Hz), 7.40-7.81 (6H, m), 7.90 (2H, d,  $J=8.4$  Hz), 8.03 (2H, d,  $J=8.4$  Hz), 8.65-8.71 (1H, m);

MASS (ES<sup>+</sup>): m/e 654.28 (M+1).

#### 35 Preparation 296

Compound (296) was obtained in a manner similar to Preparation

77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, s), 1.16-1.95 (8H, m), 1.29 (3H, s), 2.08-2.25 (2H, m), 2.25-2.42 (2H, m), 3.02 (1H, dd, J=13.6, 6.2 Hz), 3.20-3.36 (1H, m), 3.32 (1H, dd, J=13.6, 9.9 Hz), 3.81-3.93 (1H, m), 4.18-4.29 (1H, m), 4.64-4.73 (1H, m), 5.24 (1H, ddd, J=10.3, 9.9, 6.2 Hz), 5.99 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.20-7.32 (1H, m), 7.35 (2H, d, J=8.4 Hz), 7.60 (1H, d, J=10.3 Hz), 7.67-7.80 (2H, m), 7.91 (2H, d, J=8.4 Hz), 8.66-8.72 (1H, m);

MASS (ES+): m/e 550.39 (M+1).

10 Preparation 297

Compound (297) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 150.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 1.30 (3H, s), 1.38-1.94 (6H, m), 2.09-2.24 (2H, m), 2.24-2.41 (2H, m), 2.50 (2H, t, J=6.5 Hz), 3.01 (1H, dd, J=13.6, 5.9 Hz), 3.19-3.33 (1H, m), 3.31 (1H, dd, J=13.6, 10.6 Hz), 3.82-3.93 (1H, m), 4.18-4.29 (1H, m), 4.63-4.71 (1H, m), 5.23 (1H, ddd, J=10.6, 10.3, 5.9 Hz), 5.94 (1H, s), 7.16 (1H, d, J=9.9 Hz), 7.19-7.30 (1H, m), 7.35 (2H, d, J=8.4 Hz), 7.54 (1H, d, J=10.3 Hz), 7.66-7.79 (2H, m), 7.90 (2H, d, J=8.4 Hz), 8.65-8.69 (1H, m), 9.77 (1H, s);

MASS (ES+): m/e 548.30 (M+1).

Preparation 298

Compound (298) was obtained in a manner similar to Preparation 295.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.34-2.01 (8H, m), 2.07-2.41 (4H, m), 3.05 (1H, dd, J=13.9, 6.6 Hz), 3.23-3.39 (1H, m), 3.31 (1H, dd, J=13.9, 9.2 Hz), 3.82-3.94 (1H, m), 4.20-4.37 (1H, m), 4.33 (2H, t, J=6.6 Hz), 4.66-4.74 (1H, m), 5.24 (1H, ddd, J=10.6, 9.2, 6.6 Hz), 5.96 (1H, s), 7.12 (1H, d, J=10.6 Hz), 7.36 (2H, d, J=8.1 Hz), 7.40-7.72 (5H, m), 7.58 (2H, d, J=8.1 Hz), 7.63 (1H, d, J=10.6 Hz), 8.04 (2H, d, J=8.4 Hz), 8.64 (2H, d, J=5.9 Hz);

MASS (ES+): m/e 654.48 (M+1).

Preparation 299

Compound (299) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.19-1.96 (8H, m),

1.29 (3H, s), 2.05-2.40 (4H, m), 3.04 (1H, dd, J=13.9, 6.6 Hz), 3.26-3.38 (1H, m), 3.30 (1H, dd, J=13.9, 9.2 Hz), 3.66 (2H, t, J=6.3 Hz), 3.82-3.93 (1H, m), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.66-4.73 (1H, m), 5.23 (1H, s), 6.00 (1H, s), 7.10 (1H, d, J=10.3 Hz), 7.35 (2H, d, J=8.1 Hz), 7.49 (2H, d, J=5.9 Hz), 7.57 (2H, d, J=8.1 Hz), 7.62 (1H, d, J=10.3 Hz), 8.64 (2H, d, J=5.9 Hz);

MASS (ES+): m/e 550.33 (M+1).

#### Preparation 300

Compound (300) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 153.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t), 1.30 (3H, s), 1.46-1.92 (6H, m), 2.10-2.39 (4H, m), 2.50 (2H, t, J=6.2 Hz), 3.04 (1H, dd, J=13.9, 6.6 Hz), 3.21-3.38 (1H, m), 3.29 (1H, dd, J=13.9, 9.5 Hz), 3.83-3.94 (1H, m), 4.25 (1H, dt, J=10.3, 7.3 Hz), 4.65-4.74 (1H, m), 5.22 (1H, ddd, J=10.6, 9.5, 6.6 Hz), 5.99 (1H, s), 7.12 (1H, d, J=10.3 Hz), 7.36 (2H, d, J=8.4 Hz), 7.49 (2H, dd, J=4.4, 1.5 Hz), 7.56 (1H, d, J=10.6 Hz), 7.57 (2H, d, J=8.4 Hz), 8.64 (2H, dd, J=4.4, 1.5 Hz), 9.78 (1H, s);

MASS (ES+): m/e 548.28 (M+1).

#### Preparation 301

To a solution of the Compound (293) (4.02 g) in acetone (2 ml) was added t-butoxycarbonylmethyl bromide (2.65 g) and potassium carbonate (4.69 g), and the mixture was stirred at 50°C for 4 hours. The reaction mixture was extracted with ethyl acetate, washed with 5% potassium hydrogensulfate (x 2), saturated aqueous sodium bicarbonate solution, water and brine, and dried over sodium sulfate. The mixture was purified by silica gel column chromatography (eluting with hexane/ethyl acetate=1/2) to give the objective Compound (301).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.36-1.56 (2H, m), 1.48 (9H, s), 1.58-1.96 (6H, m), 2.07-2.24 (2H, m), 2.24-2.40 (2H, m), 2.89 (1H, dd, J=13.6, 5.9 Hz), 3.16-3.30 (1H, m), 3.18 (1H, dd, J=13.6, 9.6 Hz), 3.80-3.90 (1H, m), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.32 (2H, t, J=6.6 Hz), 4.47 (2H, s), 4.63-4.69 (1H, m), 5.13 (1H, ddd, J=10.3, 9.6, 5.9 Hz), 5.89 (1H, s), 6.80 (2H, d, J=8.8 Hz), 7.12-7.18 (1H, m), 7.14 (2H, d, J=8.8 Hz), 7.40-7.48 (2H, m), 7.50-7.59 (2H, m), 8.03 (2H, d, J=8.4 Hz);

MASS (ES+): m/e 707.53 (M+1).

Preparation 302

To a solution of the Compound (301) (500 mg) in methylene chloride (6 ml) was added trifluoroacetic acid (2 ml) and the mixture  
5 was stirred at ambient temperature for 2.5 hours. The solvent was evaporated in vacuo to give the objective Compound (302).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.19-1.56 (4H, m),  
1.27 (3H, s), 1.60-1.97 (4H, m), 2.03-2.23 (2H, m), 2.23-2.39 (2H, m),  
2.87 (1H, dd, J=13.9, 6.2 Hz), 3.14 (1H, dd, J=13.9, 9.5 Hz), 3.15-  
10 3.30 (1H, m), 3.62-3.89 (2H, m), 4.25 (1H, dt, J=10.5, 7.3 Hz), 4.32  
(2H, t, J=6.6 Hz), 4.62-4.71 (1H, m), 4.65 (2H, s), 5.12 (1H, ddd,  
J=10.3, 9.5, 6.2 Hz), 6.15 (1H, s), 6.83 (2H, d, J=8.4 Hz), 7.14 (2H,  
d, J=8.4 Hz), 7.25 (1H, d, J=10.3 Hz), 7.40-7.48 (2H, m), 7.52-7.60  
(1H, m), 7.64 (1H, d, J=10.3 Hz), 8.03 (2H, d, J=8.4 Hz);

15 MASS (ES+): m/e 651.51 (M+1).

Preparation 303

To a solution of the Compound (302) (405 mg) in N,N-dimethylformamide (4 ml) was added PyBOP (357 mg) and  
diisopropylethylamine (178 mg), and the mixture was stirred. To the  
20 mixture was added N-morpholine (81.6 mg) and the mixture was stirred  
at ambient temperature for 1.5 hour. The reaction mixture was  
extracted with ethyl acetate, washed with a 5% aqueous potassium  
hydrogensulfate solution (x 2), saturated aqueous sodium bicarbonate  
solution (x 2), water and brine, and dried over sodium sulfate. The  
25 mixture was purified by silica gel column chromatography (eluting with  
ethyl acetate then ethyl acetate/methanol = 9/1) to give the object  
Compound (303).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.35-  
1.98 (8H, m), 2.08-2.39 (4H, m), 2.58 (2H, t, J=7.3 Hz), 2.87-2.99 (3H,  
30 m), 3.20 (1H, dd, J=13.5, 9.2 Hz), 3.24-3.38 (3H, m), 3.46-3.55 (2H,  
m), 3.56-3.66 (4H, m), 3.83-3.93 (1H, m), 4.25 (1H, dt, J=10.3, 7.7  
Hz), 4.32 (2H, t, J=6.2 Hz), 4.65-4.71 (1H, m), 5.11-5.22 (1H, m),  
5.87 (1H, s), 7.09-7.19 (1H, m), 7.11 (2H, d, J=8.4 Hz), 7.16 (2H, d,  
J=8.4 Hz), 7.40-7.49 (2H, m), 7.53-7.60 (2H, m), 8.03 (2H, d, J=8.4  
35 Hz);

MASS (ES+): m/e 718.52 (M+1).

Preparation 304

Compound (304) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.94 (8H, m),  
5 1.28 (3H, s), 2.08-2.39 (4H, m), 2.58 (2H, t, J=7.3 Hz), 2.88-2.98 (2H,  
m), 2.94 (1H, dd, J=13.9, 6.6 Hz), 3.20 (1H, dd, J=13.9, 9.5 Hz),  
3.25-3.38 (3H, m), 3.47-3.55 (2H, m), 3.56-3.69 (4H, m), 3.65 (2H, t,  
J=6.2 Hz), 3.80-3.93 (1H, m), 4.23 (1H, dt, J=10.3, 8.1 Hz), 4.66-4.71  
(1H, m), 5.11-5.23 (1H, m), 5.96 (1H, s), 7.05-7.20 (1H, m), 7.11 (2H,  
10 d, J=8.1 Hz), 7.16 (2H, d, J=8.1 Hz), 7.56 (1H, d, J=10.3 Hz);  
MASS (ES<sup>+</sup>): m/e 614.55 (M+1).

Preparation 305

Compound (305) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 156.

15 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.46-  
1.92 (6H, m), 2.08-2.38 (4H, m), 2.45-2.54 (2H, m), 2.58 (2H, t, J=7.3  
Hz), 2.87-2.98 (3H, m), 3.20 (1H, dd, J=13.5, 9.5 Hz), 3.23-3.39 (3H,  
m), 3.45-3.55 (2H, m), 3.56-3.67 (4H, m), 3.82-3.93 (1H, m), 4.24 (1H,  
dt, J=10.3, 7.0 Hz), 4.64-4.72 (1H, m), 5.17 (1H, ddd, J=9.9, 9.5, 6.6  
20 Hz), 5.92 (1H, s), 7.08-7.19 (5H, m), 7.51 (1H, d, J=10.3 Hz), 9.77  
(1H, s);  
MASS (ES<sup>+</sup>): m/e 612.56 (M+1).

Preparation 306

Compound (306) was obtained in a manner similar to Preparation  
25 303.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (12H, s),  
1.35-1.98 (8H, m), 2.06-2.36 (4H, m), 2.34 (2H, t, J=7.7 Hz), 2.89 (2H,  
t, J=7.7 Hz), 2.92 (1H, dd, J=13.5, 6.2 Hz), 3.21 (1H, dd, J=13.5, 9.9  
Hz), 3.22-3.33 (1H, m), 3.81-3.92 (1H, m), 4.24 (1H, dt, J=10.6, 7.7  
30 Hz), 4.32 (2H, t, J=6.6 Hz), 4.64-4.71 (1H, m), 5.10 (1H, s), 5.16 (1H,  
ddd, J=9.9, 9.9, 5.9 Hz), 5.85 (1H, s), 7.07-7.20 (1H, m), 7.09 (2H, d,  
J=8.4 Hz), 7.14 (2H, d, J=8.4 Hz), 7.40-7.49 (2H, m), 7.51-7.60 (2H,  
m), 8.03 (2H, d, J=8.4 Hz);  
MASS (ES<sup>+</sup>): m/e 704.53 (M+1).

35 Preparation 307

Compound (307) was obtained in a manner similar to Preparation

77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.23-1.90 (8H, m), 1.28 (12H, s), 2.10-2.37 (4H, m), 2.58 (2H, t, J=8.4 Hz), 2.93 (2H, t, J=8.4 Hz), 2.95 (1H, dd, J=13.9, 6.2 Hz), 3.20 (1H, dd, J=13.9, 9.5 Hz), 3.27-3.39 (3H, m), 3.47-3.55 (2H, m), 3.56-3.69 (4H, m), 3.66 (2H, t, J=6.2 Hz), 3.82-3.93 (1H, m), 4.23 (1H, dt, J=10.3, 7.7 Hz), 4.66-4.71 (1H, m), 5.17 (1H, ddd, J=10.3, 9.5, 6.6 Hz), 5.96 (1H, s), 7.06-7.18 (1H, m), 7.11 (2H, d, J=8.1 Hz), 7.16 (2H, d, J=8.1 Hz), 7.55 (1H, d, J=10.3 Hz);

10 MASS (ES+): m/e 600.57 (M+1).

Preparation 308

Compound (308) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 159.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.28 (12H, s), 1.42-1.90 (6H, m), 2.09-2.40 (4H, m), 2.34 (2H, t, J=7.3 Hz), 2.46-2.61 (2H, m), 2.88 (2H, t, J=7.3 Hz), 2.93 (1H, dd, J=13.9, 6.2 Hz), 3.20 (1H, dd, J=13.9, 9.2 Hz), 3.22-3.38 (1H, m), 3.82-3.92 (1H, m), 4.23 (1H, dt, J=9.9, 7.3 Hz), 4.64-4.71 (1H, m), 5.10 (1H, s), 5.16 (1H, ddd, J=10.6, 9.2, 6.2 Hz), 5.91 (1H, s), 7.07-7.18 (1H, m), 7.10 (2H, d, J=8.1 Hz), 7.14 (2H, d, J=8.1 Hz), 7.49 (1H, d, J=9.9 Hz), 9.77 (1H, s);

20 MASS (ES+): m/e 598.59 (M+1).

Preparation 309

To a solution of the Compound (293) (148 mg) in a mixed solvent of carbon tetrachloride/acetonitrile/water (0.4, 0.4 and 0.6 ml) was added sodium periodate (758 mg) and the mixture was stirred. To the mixture was added ruthenium(IV) oxide catalyst (0.665 mg) and the mixture was stirred at ambient temperature for 36 hours. To the reaction mixture was added ethyl acetate and the insoluble matter was filtered off. The mixture was extracted with water and ethyl acetate, and the organic layer was evaporated. The residue was purified by preparative chromatography (chloroform/methanol = 9/1) to give the objective Compound (309).

25 30

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.34-2.44 (12H, m), 2.65 (1H, dd, J=17.2, 3.7 Hz), 3.18 (1H, dd, J=17.2, 10.3 Hz), 3.71 (1H, dt, J=9.9, 7.0 Hz), 3.84-3.95 (1H, m), 4.26 (1H,

35

dt, J=10.3, 7.7 Hz), 4.31 (2H, t, J=6.6 Hz), 4.69-4.76 (1H, m), 5.28 (1H, ddd, J=10.3, 10.3, 3.7 Hz), 5.97 (1H, s), 7.08 (1H, d, J=10.3 Hz), 7.40-7.48 (1H, m), 7.52-7.60 (1H, m), 7.60 (1H, d, J=10.3 Hz), 8.03 (2H, d, J=8.4 Hz);

5 MASS (ES+): m/e 545.49 (M+1).

#### Preparation 310

Compound (310) was obtained in a manner similar to Preparation 303.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.34-2.42 (12H, m),  
10 1.30 (3H, s), 2.72 (1H, dd, J=15.4, 4.4 Hz), 3.21 (1H, dd, J=15.4, 10.9 Hz), 3.81 (1H, dt, J=10.3, 7.7 Hz), 3.92 (1H, dt, J=10.3, 4.8 Hz), 4.26 (1H, dt, J=9.9, 8.1 Hz), 4.31 (2H, t, J=6.6 Hz), 4.68-4.74 (1H, m), 5.44 (1H, ddd, J=10.9, 10.6, 4.4 Hz), 5.94 (1H, s), 7.09 (1H, d, J=10.6 Hz), 7.11 (1H, dd, J=7.7, 7.7 Hz), 7.30 (2H, dd, J=8.1, 7.7 Hz),  
15 7.39-7.47 (4H, m), 7.50 (1H, d, J=9.9 Hz), 7.51-7.61 (2H, m), 8.03 (2H, d, J=8.4 Hz);

MASS (ES+): m/e 620.51 (M+1).

#### Preparation 311

Compound (311) was obtained in a manner similar to Preparation  
20 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 1.18-2.43 (12H, m),  
1.31 (9H, s), 2.73 (1H, dd, J=15.4, 4.4 Hz), 3.20 (1H, dd, J=15.4, 10.6 Hz), 3.65 (2H, t, J=6.2 Hz), 3.82 (1H, dt, J=10.3, 7.7 Hz), 3.92 (1H, dt, J=10.3, 4.4 Hz), 4.25 (1H, dt, J=10.3, 7.7 Hz), 4.68-4.76 (1H, m),  
25 5.44 (1H, ddd, J=11.0, 10.6, 4.4 Hz), 6.12 (1H, s), 7.10 (1H, dd, J=7.3, 7.3 Hz), 7.11 (1H, d, J=10.3 Hz), 7.30 (2H, dd, J=7.7, 7.3 Hz), 7.44 (2H, d, J=7.7 Hz), 7.51 (1H, d, J=11.0 Hz), 7.55-7.65 (1H, m);

MASS (ES+): m/e 516.56 (M+1).

#### Preparation 312

Compound (312) was obtained in a manner similar to Preparation  
30 78. The obtained compound was used in Example 166.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 1.31 (3H, s), 1.35-2.42 (10H, m), 2.49 (2H, t, J=7.0 Hz), 2.72 (1H, dd, J=15.4, 4.4 Hz), 3.20 (1H, dd, J=15.4, 11.0 Hz), 3.81 (1H, dt, J=10.3, 7.0 Hz), 3.93  
35 (1H, dt, J=10.3, 5.1 Hz), 4.25 (1H, dt, J=9.9, 7.7 Hz), 4.67-4.74 (1H, m), 5.44 (1H, ddd, J=11.0, 10.6, 4.4 Hz), 5.98 (1H, s), 7.05-7.14 (2H,

m), 7.30 (2H, dd, J=8.1, 7.7 Hz), 7.38-7.49 (2H, m), 7.44 (2H, d, J=8.1 Hz), 9.76 (1H, s);

MASS (ES+): m/e 514.52 (M+1).

#### Preparation 313

5           Compound (313) was obtained in a manner similar to Preparation 303.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.38-1.98 (8H, m), 2.07-2.38 (4H, m), 2.93 (1H, dd, J=13.9, 6.2 Hz), 3.20 (1H, dd, J=13.9, 9.5 Hz), 3.22-3.34 (1H, m), 3.81-3.91 (1H, m), 4.25 (1H, dt, J=10.3, 7.3 Hz), 4.32 (2H, t, J=6.6 Hz), 4.58 (2H, s), 4.64-4.71 (1H, m), 5.14 (1H, ddd, J=10.3, 9.5, 6.2 Hz), 5.88 (1H, s), 6.91 (2H, d, J=8.4 Hz), 7.11 (1H, d, J=9.9 Hz), 7.16 (1H, dd, J=7.7, 7.7 Hz), 7.21 (2H, d, J=8.4 Hz), 7.36 (2H, dd, J=7.7, 7.3 Hz), 7.40-7.49 (2H, m), 7.53-7.62 (2H, m), 7.58 (2H, d, J=7.3 Hz), 8.03 (2H, d, J=8.4 Hz), 8.24 (1H, brs);

MASS (ES+): m/e 726.52 (M+1).

#### Preparation 314

Compound (314) was obtained in a manner similar to Preparation 77.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t), 1.18-1.92 (8H, m), 1.28 (3H, s), 2.08-2.39 (4H, m), 2.93 (1H, dd, J=13.9, 6.6 Hz), 3.19 (1H, dd, J=13.9, 9.2 Hz), 3.21-3.34 (1H, m), 3.60-3.70 (2H, m), 3.80-3.90 (1H, m), 4.23 (1H, dt, J=10.3, 7.7 Hz), 4.58 (2H, s), 4.64-4.71 (1H, m), 5.14 (1H, ddd, J=9.9, 9.2, 6.6 Hz), 5.90 (1H, s), 6.91 (2H, d, J=8.4 Hz), 7.09 (1H, d, J=10.3 Hz), 7.16 (2H, dd, J=7.3, 7.3 Hz), 7.21 (2H, d, J=8.4 Hz), 7.36 (2H, dd, J=7.3, 7.3 Hz), 7.55 (1H, d, J=9.9 Hz), 7.57 (2H, d, J=7.3 Hz), 8.24 (1H, brs);

MASS (ES+): m/e 622.54 (M+1).

#### Preparation 315

30           Compound (315) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 169.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.48-1.91 (6H, m), 2.09-2.39 (4H, m), 2.45-2.54 (2H, m), 2.93 (1H, dd, J=13.5, 6.6 Hz), 3.19 (1H, dd, J=13.5, 9.6 Hz), 3.22-3.33 (1H, m), 3.81-3.91 (1H, m), 4.23 (1H, dt, J=10.6, 7.3 Hz), 4.64-4.72 (1H, m), 5.14 (1H, ddd, J=9.9, 9.6, 6.6 Hz), 5.89 (1H, s), 6.91 (2H, d, J=8.4

Hz), 7.12 (1H, d, J=10.6 Hz), 7.15 (1H, dd, J=7.3, 7.3 Hz), 7.21 (2H, d, J=8.4 Hz), 7.36 (2H, dd, J=7.7, 7.3 Hz), 7.51 (1H, d, J=9.9 Hz), 7.58 (2H, d, J=7.7 Hz), 8.24 (1H, brs), 9.77 (1H, s);  
MASS (ES+): m/e 620.53 (M+1).

5 Preparation 316

Compound (316) was obtained in a manner similar to Preparation 313.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 0.89 (3H, t, J=7.0 Hz), 1.20-1.98 (14H, m), 1.27 (3H, s), 2.01-2.39 (4H, m), 2.91 (1H, dd, J=13.5, 6.2 Hz), 3.18 (1H, dd, J=13.5, 9.2 Hz), 3.21-3.37 (3H, m), 3.80-3.91 (1H, m), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.32 (2H, t, J=6.6 Hz), 4.44 (2H, s), 4.65-4.71 (1H, m), 5.13 (1H, ddd, J=10.6, 9.2, 6.2 Hz), 5.85 (1H, s), 6.55 (1H, br), 6.83 (2H, d, J=8.4 Hz), 7.10 (1H, d, J=10.6 Hz), 7.18 (2H, d, J=8.4 Hz), 7.40-7.48 (2H, m), 7.53-7.60 (1H, m), 7.57 (1H, d, J=10.3 Hz), 8.03 (2H, d, J=8.4 Hz);  
MASS (ES+): m/e 720.53 (M+1).

Preparation 317

Compound (317) was obtained in a manner similar to Preparation 77.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 0.89 (3H, t, J=6.6 Hz), 1.22-1.93 (14H, m), 1.28 (3H, s), 2.07-2.41 (4H, m), 2.91 (1H, dd, J=13.5, 6.2 Hz), 3.18 (1H, dd, J=13.5, 9.2 Hz), 3.23-3.38 (3H, m), 3.66 (2H, t, J=6.2 Hz), 3.86 (1H, dt, J=8.8, 4.8 Hz), 4.23 (1H, dt, J=10.3, 7.7 Hz), 4.44 (2H, s), 4.65-4.71 (1H, m), 5.13 (1H, ddd, J=10.3, 9.2, 6.2 Hz), 5.96 (1H, s), 6.55 (1H, br), 6.83 (2H, d, J=8.4 Hz), 7.10 (1H, d, J=10.3 Hz), 7.17 (2H, d, J=8.4 Hz), 7.55 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 616.60 (M+1).

Preparation 318

30 Compound (318) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 172.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 0.89 (3H, t, J=7.7 Hz), 1.05-1.40 (4H, m), 1.29 (3H, s), 1.42-1.94 (6H, m), 2.08-2.41 (4H, m), 2.46-2.55 (2H, m), 2.91 (1H, dd, J=13.9, 5.9 Hz), 3.18 (1H, dd, J=13.9, 9.5 Hz), 3.20-3.37 (3H, m), 3.81-3.91 (1H, m), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.44 (2H, s), 4.64-4.72 (1H, m), 5.13 (1H, ddd, J=9.9,

9.5, 5.9 Hz), 5.94 (1H, s), 6.56 (1H, br), 6.83 (2H, d, J=8.1 Hz), 7.13 (1H, d, J=10.3 Hz), 7.18 (2H, d, J=8.1 Hz), 7.51 (1H, d, J=9.9 Hz), 9.78 (1H, s);

MASS (ES+): m/e 614.61 (M+1).

5 Preparation 319

Compound (319) was obtained in a manner similar to Example 141 mentioned below.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.33-1.99 (12H, m), 2.05-2.40 (6H, m), 2.90 (1H, dd, J=13.6, 6.2 Hz), 3.18  
10 (1H, dd, J=13.6, 9.2 Hz), 3.22-3.33 (1H, m), 3.54-3.70 (4H, m), 3.80-3.91 (1H, m), 4.18-4.33 (1H, m), 4.32 (2H, t, J=6.2 Hz), 4.65-4.70 (1H, m), 4.66 (2H, s), 5.13 (1H, dt, J=9.9, 6.2 Hz), 5.81 (1H, s), 6.84 (2H, d, J=8.8 Hz), 7.08-7.19 (3H, m), 7.40-7.48 (2H, m), 7.50-7.60 (2H, m), 8.00-8.06 (2H, m);

15 MASS (ES+): m/e 718.38 (M+1).

Preparation 320

Compound (320) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.17-1.93 (14H, m),  
20 1.28 (3H, s), 2.07-2.39 (4H, m), 2.88 (1H, dd, J=13.5, 6.2 Hz), 3.18 (1H, dd, J=13.5, 9.9 Hz), 3.20-3.31 (1H, m), 3.42-3.50 (2H, m), 3.51-3.60 (2H, m), 3.66 (2H, t, J=6.6 Hz), 3.79-3.91 (1H, m), 4.23 (1H, dt, J=9.9, 7.7 Hz), 4.64 (2H, s), 4.65-4.71 (1H, m), 5.13 (1H, ddd, J=10.3, 9.9, 6.2 Hz), 5.92 (1H, s), 6.85 (2H, d, J=8.4 Hz), 7.13 (1H, d, J=9.9  
25 Hz), 7.14 (2H, d, J=8.4 Hz), 7.54 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 614.55 (M+1).

Preparation 321

Compound (321) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 175.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.46-  
30 1.91 (12H, m), 2.03-2.40 (4H, m), 2.45-2.54 (2H, m), 2.88 (1H, dd, J=13.5, 6.2 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.20-3.31 (1H, m), 3.42-3.50 (2H, m), 3.51-3.59 (2H, m), 3.79-3.90 (1H, m), 4.23 (1H, dt, J=9.9, 7.0 Hz), 4.64 (2H, s), 4.65-4.70 (1H, m), 5.13 (1H, ddd, J=10.3,  
35 9.5, 6.2 Hz), 5.89 (1H, s), 6.85 (2H, d, J=8.8 Hz), 7.14 (2H, d, J=8.8 Hz), 7.14 (1H, d, J=9.9 Hz), 7.48 (1H, d, J=10.3 Hz), 9.77 (1H, s);

MASS (ES+): m/e 612.60 (M+1).

Preparation 322

To a solution of the Compound (294) (500 mg) in dioxane (6 ml) and water (2 ml) was added a 2M aqueous solution of sodium carbonate (2 ml), and the solution was stirred. To the mixture were added 3-pyridinylboronic acid (170 mg) and dichlorobis(trichlorophosphine)palladium (II) catalyst (48.4 mg). The obtained suspension was degassed with ultrasonic for 1 to 2 min, and the air was purged from the reaction vessel with nitrogen. The suspension was stirred at 95°C for 1 hour, then cooled to ambient temperature and extracted with ethyl acetate. The extract was washed with water and brine, dried over sodium sulfate and filtered. The filtrate was evaporated and the residue was purified with silica gel column chromatography (eluting with ethyl acetate, then ethyl acetate/methanol = 9/1) to give the objected Compound (322).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.34-1.99 (8H, m), 2.08-2.38 (4H, m), 3.04 (1H, dd, J=13.6, 6.2 Hz), 3.27-3.39 (1H, m), 3.29 (1H, dd, J=13.6, 9.2 Hz), 3.84-3.94 (1H, m), 4.20-4.30 (1H, m), 4.32 (2H, t, J=6.6 Hz), 4.67-4.73 (1H, m), 5.23 (1H, ddd, J=10.3, 9.2, 6.2 Hz), 5.89 (1H, s), 7.11 (1H, d, J=10.6 Hz), 7.32-7.39 (1H, m), 7.35 (2H, d, J=8.4 Hz), 7.40-7.72 (6H, m), 7.83-7.89 (1H, m), 8.03 (2H, d, J=8.4 Hz), 8.56-8.60 (1H, m), 8.81-8.85 (1H, m);

MASS (ES+): m/e 654.50 (M+1).

Preparation 323

Compound (323) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.25-1.94 (8H, m), 1.29 (3H, s), 2.11-2.26 (2H, m), 2.26-2.40 (2H, m), 3.04 (1H, dd, J=13.5, 6.2 Hz), 3.29 (1H, dd, J=13.5, 9.2 Hz), 3.30-3.39 (1H, m), 3.62-3.70 (2H, m), 3.84-3.94 (1H, m), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.67-4.73 (1H, m), 5.23 (1H, ddd, J=10.3, 9.2, 6.2 Hz), 5.97 (1H, s), 7.11 (1H, d, J=10.3 Hz), 7.35 (2H, d, J=8.4 Hz), 7.36 (1H, dd, J=7.7, 0.7 Hz), 7.51 (2H, d, J=8.4 Hz), 7.61 (1H, d, J=10.3 Hz), 7.83-7.88 (1H, m), 8.57 (1H, dd, J=4.8, 1.5 Hz), 8.81-8.84 (1H, m);

MASS (ES+): m/e 550.52 (M+1).

Preparation 324

Compound (324) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 178.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.30 (3H, s), 1.46-1.93 (6H, m), 2.10-2.39 (4H, m), 2.46-2.55 (2H, m), 3.04 (1H, dd, J=13.6, 6.6 Hz), 3.26-3.38 (1H, m), 3.28 (1H, dd, J=13.6, 9.5 Hz), 3.85-3.94 (1H, m), 4.25 (1H, dt, J=10.3, 7.3 Hz), 4.67-4.73 (1H, m), 5.23 (1H, ddd, J=10.3, 9.5, 6.6 Hz), 5.94 (1H, s), 7.13 (1H, d, J=10.3 Hz), 7.35 (2H, d, J=8.4 Hz), 7.36 (1H, d, J=7.7 Hz), 7.51 (2H, d, J=8.4 Hz), 7.56 (1H, d, J=10.3 Hz), 7.83-7.88 (1H, m), 8.58 (1H, dd, J=4.8, 1.8 Hz), 8.81-8.84 (1H, m), 9.78 (1H, s);  
MASS (ES+): m/e 548.46 (M+1).

#### Preparation 325

(2S)-2-amino-3-(3,4-dichlorophenyl)propanoic acid (3.17 g) and sodium bicarbonate (2.28 g) was added to a mixed solvent of dioxane and water (20 ml/20 ml). To the mixture was added Boc<sub>2</sub>O (5.91 g) and the mixture was stirred at ambient temperature for 6 hours. To the mixture was added water and the mixture was extracted with ether. The water layer was adjusted to pH 2 with hydrochloric acid and extracted with ethyl acetate. The extract was washed with water and brine, and dried over sodium sulfate. The solvent was removed by evaporation to give the objective Compound (325).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.32 (3H, s), 1.43 (6H, s), 2.81-3.08 (1H, m), 3.09-3.26 (1H, m), 4.51-4.64 (1H, m), 4.94-5.05 (1H, m), 7.03 (1H, dd, J=8.4, 2.2 Hz), 7.25-7.34 (1H, m), 7.37 (1H, d, J=8.4 Hz);  
MASS (ES-): m/e 332.16 (M-1).

#### Preparation 326

Compound (326) was obtained in a manner similar to Preparation 13.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.34 (2H, s), 1.42 (7H, s), 1.65-1.79 (1H, m), 1.84-2.30 (3H, m), 2.81-3.02 (2.5H, m), 3.54-3.69 (1.5H, m), 4.36-4.47 (1H, m), 4.55-4.67 (1H, m), 5.10 (1H, d, J=12.5 Hz), 5.22 (1H, d, J=12.5 Hz), 5.30 (1H, d, J=8.8 Hz), 7.07 (1H, dd, J=8.1, 1.8 Hz), 7.22-7.41 (6H, m), 7.29 (1H, d, J=1.8 Hz);  
MASS (ES+): m/e 521.31 (M+1).

#### Preparation 327

Compound (327) was obtained in a manner similar to Preparation

14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.39 (3H, s), 1.43 (9H, s), 1.50-2.34 (6H, m), 2.88-3.04 (2.5H, m), 3.46-3.70 (1.5H, m), 4.39-4.46 (1H, m), 4.69-5.06 (2H, m), 5.10 (1H, d, J=12.4 Hz), 5.18 (1H, d, J=12.4 Hz), 6.86 (1H, d, J=8.4 Hz), 7.10 (1H, dd, J=8.4, 2.2 Hz), 7.28-7.40 (7H, m);

MASS (ES<sup>+</sup>): m/e 620.41 (M+1).

Preparation 328

Compound (328) was obtained in a manner similar to Preparation

10 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.75 (3H, t, J=7.3 Hz), 1.34-2.34 (12H, m), 1.44 (9H, s), 1.47 (3H, s), 2.86-3.09 (0.5H, m), 2.91 (1H, dd; J=13.2, 5.9 Hz), 3.02 (1H, dd, J=13.2, 8.4 Hz), 3.51-3.72 (1.5H, m), 3.90-4.10 (1H, m), 4.32 (2H, t, J=6.2 Hz), 4.39-4.46 (1H, m), 4.83-5.06 (2H, m), 5.06-5.23 (2H, m), 6.79-6.95 (1H, m), 6.86 (1H, s), 7.07 (1H, dd, J=8.4, 2.2 Hz), 7.19-7.38 (7H, m), 7.39-7.47 (2H, m), 7.51-7.59 (1H, m), 8.03 (2H, d, J=7.0 Hz);

MASS (ES<sup>+</sup>): m/e 853.59 (M+1).

Preparation 329

20 Compound (329) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.3 Hz), 1.45 (12H, s), 1.58-2.00 (12H, m), 2.11-2.25 (0.5H, m), 2.81-3.10 (3.5H, m), 3.78-3.92 (1H, m), 4.21-4.43 (3H, m), 4.83-4.93 (1H, m), 5.52-5.63 (1H, m), 6.77 (1H, s), 7.08 (1H, dd, J=8.4, 1.8 Hz), 7.18-7.28 (1H, m), 7.31 (1H, d, J=1.8 Hz), 7.36 (1H, d, J=8.4 Hz), 7.39-7.48 (2H, m), 7.52-7.59 (1H, m), 8.03 (2H, d, J=7.0 Hz);

MASS (ES<sup>+</sup>): m/e 763.52 (M+1).

Preparation 330

30 Compound (330) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, br), 1.37 (3H, s), 1.50-2.15 (13H, m), 2.75-2.93 (1H, m), 2.94-3.10 (1H, m), 3.11-3.27 (1H, m), 3.65-3.80 (1H, m), 3.97-4.40 (3H, m), 4.83-4.98 (1H, m), 7.00-7.12 (1H, m), 7.27-7.35 (2H, m), 7.35-7.45 (2H, m), 7.49-7.57 (1H, m), 7.62-7.78 (1H, m), 7.99 (2H, d, J=7.3 Hz), 8.03-8.22 (2H, m);

MASS (ES+): m/e 663.45 (M+1).

Preparation 331

Compound (331) was obtained in a manner similar to Preparation 76.

5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.35-1.56 (2H, m), 1.60-1.98 (6H, m), 2.11-2.38 (4H, m), 2.93 (1H, dd, J=13.9, 6.2 Hz), 3.16 (1H, dd, J=13.9, 9.2 Hz), 3.26-3.37 (1H, m), 3.76-3.89 (1H, m), 4.18-4.49 (1H, m), 4.31 (2H, t, J=6.3 Hz), 4.65-4.73 (1H, m), 5.06-5.17 (1H, m), 6.01 (1H, s), 7.07 (1H, dd, J=8.1, 2.2 Hz), 7.09 (1H, d, J=9.9 Hz), 7.29-7.37 (2H, m), 7.38-7.48 (2H, m), 7.51-7.60 (1H, m), 7.64 (1H, d, J=10.3 Hz), 8.02 (2H, d, J=7.0 Hz);  
10 MASS (ES+): m/e 645.42 (M+1).

Preparation 332

Compound (332) was obtained in a manner similar to Preparation 15 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.30-1.52 (2H, m), 1.54-2.00 (6H, m), 2.08-2.38 (4H, m), 2.93 (1H, dd, J=13.6, 6.6 Hz), 3.16 (1H, dd, J=13.6, 8.8 Hz), 3.32 (1H, dt, J=9.9, 7, 3 Hz), 3.66 (1H, t, J=6.2 Hz), 3.79-3.89 (1H, m), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.66-4.72 (1H, m), 5.12 (1H, ddd, J=10.3, 8.8, 6.6 Hz), 6.02 (1H, s), 7.05 (1H, d, J=10.3 Hz), 7.07 (1H, dd, J=8.1, 2.2 Hz), 7.35 (1H, d, J=8.1 Hz), 7.61 (1H, d, J=10.3 Hz);  
20 MASS (ES+): m/e 541.38 (M+1).

Preparation 333

25 Compound (333) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 181.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.48-1.93 (6H, m), 2.10-2.42 (4H, m), 2.46-2.55 (2H, m), 2.93 (1H, dd, J=13.5, 6.6 Hz), 3.16 (1H, dd, J=13.5, 9.2 Hz), 3.27-3.37 (1H, m), 30 3.81-3.91 (1H, m), 4.25 (1H, dt, J=10.3, 7.7 Hz), 4.66-4.72 (1H, m), 5.12 (1H, ddd, J=9.9, 9.2, 6.6 Hz), 5.89 (1H, s), 7.04 (1H, d, J=9.9 Hz), 7.08 (1H, dd, J=8.1, 2.2 Hz), 7.34 (1H, d, J=2.2 Hz), 7.35 (1H, d, J=8.1 Hz), 7.55 (1H, d, J=10.3 Hz), 9.77 (1H, s);  
MASS (ES+): m/e 539.32 (M+1).

35 Preparation 334

Compound (334) was obtained in a manner similar to Preparation

14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.34-1.64 (4H, m), 1.48 (9H, s), 1.64-1.77 (1H, m), 3.04-3.17 (1H, m), 3.31 (1H, dd, J=12.8, 11.0 Hz), 3.69 (1H, dd, J=12.8, 4.4 Hz), 4.01-4.13 (1H, m), 4.76 (1H, ddd, J=11.0, 8.1, 4.4 Hz), 5.05 (1H, d, J=12.1 Hz), 5.17 (1H, d, J=12.1 Hz), 5.59 (1H, d, J=8.1 Hz), 7.17-7.43 (7H, m), 7.48 (1H, dd, J=8.4, 7.3 Hz), 7.59 (1H, dd, J=8.4, 7.3 Hz), 7.73 (1H, d, J=7.3 Hz), 7.82 (1H, d, J=7.3 Hz), 8.23 (1H, d, J=8.4 Hz);  
MASS (ES+): m/e 503.22 (M+1).

10 Preparation 335

Compound (335) was obtained in a manner similar to Preparation

15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.3 Hz), 1.32-1.63 (4H, m), 1.45 (9H, s), 1.47 (3H, s), 1.63-1.75 (1H, m), 1.86-2.08 (2H, m), 3.02-3.13 (1H, m), 3.22 (1H, dd, J=12.8, 11.0 Hz), 3.77 (1H, dd, J=12.8, 4.0 Hz), 4.10-4.19 (1H, m), 5.00-5.19 (2H, m), 5.06 (1H, d, J=12.5 Hz), 5.13 (1H, d, J=12.5 Hz), 7.08 (1H, d, J=7.7 Hz), 7.20-7.41 (7H, m), 7.43-7.54 (1H, m), 7.56-7.65 (1H, m), 7.74 (1H, dd, J=6.6, 2.6 Hz), 7.82 (1H, d, J=8.4 Hz), 8.36 (1H, d, J=8.4 Hz);  
MASS (ES+): m/e 602.51 (M+1).

20 Preparation 336

Compound (336) was obtained in a manner similar to Preparation

16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.3 Hz), 1.15-2.39 (13H, m), 1.44 (2H, s), 1.46 (7H, s), 1.56 (3H, s), 3.09-3.19 (1H, m), 3.28 (1H, dd, J=12.8, 10.6 Hz), 3.70 (1H, dd, J=12.8, 4.4 Hz), 4.05-4.20 (1H, m), 4.33 (2H, t, J=6.2 Hz), 5.01-5.21 (2H, m), 5.07 (1H, d, J=12.5 Hz), 5.13 (1H, d, J=12.5 Hz), 6.94 (1H, d, J=7.7 Hz), 7.07 (1H, s), 7.25-7.39 (7H, m), 7.38-7.48 (1H, m), 7.48-7.64 (2H, m), 7.71-7.78 (1H, m), 7.83 (1H, d, J=7.7 Hz), 8.03 (2H, d, J=8.4 Hz), 8.29 (1H, d, J=8.4 Hz);  
MASS (ES+): m/e 835.45 (M+1).

30 Preparation 337

Compound (337) was obtained in a manner similar to Preparation

35 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.03-2.08 (13H, m),

1.44 (3H, s), 1.45 (6H, s), 1.57 (3H, s), 3.10-3.41 (2H, m), 3.59-3.73 (1H, m), 4.00-4.19 (1H, m), 4.25-4.40 (3H, m), 5.02-5.42 (2H, m), 6.88 (1H, s), 7.26-7.64 (6H, m), 7.72-7.80 (1H, m), 7.84 (1H, d, J=8.1 Hz), 8.04 (2H, d, J=8.4 Hz), 8.24 (1H, d, J=8.8 Hz);

5 MASS (ES+): m/e 745.41 (M+1).

Preparation 338

Compound (338) was obtained in a manner similar to Preparation 18.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72-0.88 (3H, m), 1.10-2.32 (14H, m), 1.43 (3H, s), 3.29-3.63 (2H, m), 3.98-4.08 (1H, m), 4.18-4.43 (3H, m), 5.01-5.18 (1H, m), 7.21-7.59 (6H, m), 7.60-7.75 (1H, m), 7.79 (1H, d, J=8.4 Hz), 7.99 (1H, d, J=7.7 Hz), 8.09-8.65 (4H, m);

MASS (ES+): m/e 645.32 (Free).

Preparation 339

15 Compound (339) was obtained in a manner similar to Preparation 76.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.36-2.03 (8H, m), 2.05-2.20 (2H, m), 2.22-2.40 (2H, m), 3.05 (1H, dt, J=9.9, 7.7 Hz), 3.50 (1H, dd, J=14.3, 6.2 Hz), 3.64 (1H, dd, J=14.3, 9.2 Hz), 3.75 (1H, dt, J=9.9, 4.8 Hz), 4.18-4.32 (1H, m), 4.33 (2H, t, J=6.6 Hz), 4.62-4.71 (1H, m), 5.43 (1H, ddd, J=10.3, 9.2, 6.2 Hz), 5.82 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.35-7.62 (7H, m), 7.66 (1H, d, J=10.3 Hz), 7.70-7.77 (1H, m), 7.85 (1H, d, J=8.1 Hz), 8.04 (2H, d, J=8.4 Hz), 8.13 (1H, d, J=8.8 Hz);

25 MASS (ES+): m/e 627.44 (M+1).

Preparation 340

Compound (340) was obtained in a manner similar to Preparation 77.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.30-1.96 (8H, m), 2.07-2.22 (2H, m), 2.23-2.38 (2H, m), 3.05 (1H, dt, J=10.3, 7.7 Hz), 3.50 (1H, dd, J=13.9, 6.6 Hz), 3.57-3.71 (2H, m), 3.64 (1H, dd, J=13.9, 9.2 Hz), 3.75 (1H, dt, J=10.3, 4.4 Hz), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.61-4.70 (1H, m), 5.43 (1H, ddd, J=10.3, 9.2, 6.6 Hz), 5.95 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.34-7.41 (2H, m), 35 7.45-7.53 (1H, m), 7.53-7.61 (1H, m), 7.66 (1H, d, J=10.3 Hz), 7.70-7.77 (1H, m), 7.85 (1H, d, J=8.1 Hz), 8.13 (1H, d, J=8.4 Hz);

MASS (ES+): m/e 523.41 (M+1).

Preparation 341

Compound (341) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 184.

5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.43-1.95 (6H, m), 2.06-2.36 (4H, m), 2.51 (1H, dt, J=6.2, 1.1 Hz), 3.03 (1H, dt, J=9.9, 7.7 Hz), 3.50 (1H, dd, J=14.3, 6.2 Hz), 3.63 (1H, dd, J=14.3, 9.2 Hz), 3.74 (1H, dt, J=9.9, 4.4 Hz), 4.24 (1H, dt, J=10.3, 7.0 Hz), 4.61-4.70 (1H, m), 5.42 (1H, ddd, J=9.9, 9.2, 6.2 Hz), 5.90  
10 (1H, s), 7.16 (1H, d, J=10.3 Hz), 7.33-7.41 (2H, m), 7.45-7.61 (2H, m), 7.60 (1H, d, J=9.9 Hz), 7.70-7.77 (1H, m), 7.85 (1H, d, J=8.1 Hz), 8.12 (1H, d, J=8.4 Hz), 9.78 (1H, t, J=1.1 Hz);  
MASS (ES+): m/e 521.33 (M+1).

Preparation 342

15 The Compound (294) (9.83 g) was dissolved in N,N-dimethylformamide (100 ml), and lithium chloride (4.02 g), tributylvinyltin (5.16 g) and dichlorobis(triphenylphosphine)palladium (II) (476 mg) were added to the mixture under nitrogen atmosphere. The mixture was stirred at 100°C for 1 day. The reaction mixture was  
20 cooled to room temperature, and an aqueous solution of hydrogen fluoride (16 g in water (15 ml)) was added to the mixture and stirred for 60 min. The reaction mixture was diluted with ethyl acetate and the insoluble matter was filtered off. The mixture was partitioned between ethyl acetate and water, and the ethyl acetate layer was  
25 washed with an aqueous solution of hydrogen fluoride (10 g in water (100 ml)), water and saturated brine, dried over sodium sulfate and evaporated. The residue was purified by flush chromatography (Silica gel 60N, Spherical, eluting with ethyl acetate/hexane = 1/1 then 2/1) to give the objective Compound (342) as a pale yellow foam.  
30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.4 Hz), 1.28 (3H, s), 1.36-1.54 (2H, m), 1.67-1.99 (4H, m), 2.08-2.40 (4H, m), 2.95 (1H, dd, J=13.5, 6 Hz), 3.23 (1H, dd, J=13.5, 9.5 Hz), 3.28 (1H, m), 3.86 (1H, m), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.32 (2H, t, J=6.3 Hz), 4.67 (1H, m), 5.18 (1H, m), 5.21 (1H, d, J=10.8 Hz), 5.71 (1H, d, J=17.6 Hz),  
35 5.87 (1H, s), 6.68 (1H, dd, J=17.6, 10.8 Hz), 7.13 (1H, d, J=10.3 Hz), 7.19 (2x1H, d, J=8.1 Hz), 7.32 (2x1H, d, J=8.1 Hz), 7.44 (2x1H, dd,

J=7.5, 7.5 Hz), 7.52-7.60 (2H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);  
MASS (ES+): m/e 603.51.

Preparation 343

The Compound (342) was dissolved into a mixed solvent of  
5 methanol/dichloromethane (2/1, 60 ml), and the mixture was cooled in  
dry ice-acetone bath (internal temperature: about 70°C) and bubbled  
with 1 to 2% of ozone in oxygen at the velocity of 1L/min for 15 min.  
The mixture was stirred under nitrogen atmosphere and then under  
oxygen atmosphere. To the mixture was added dimethyl sulfide (0.7 ml)  
10 and the mixture was stirred with raising the temperature to ambient  
temperature. The reaction mixture was evaporated and purified by  
flash column chromatography (Silica gel 60N, Spherical, 110g, eluting  
with ethyl acetate/hexane = 1/1, 3/2, then 2/1) and preparative thin  
layer chromatography (eluting with ethyl acetate/hexane = 1/1 then  
15 methanol/chloroform = 1/20) to give the objective Compound (343).  
<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.36-  
1.55 (2H, m), 1.58-1.99 (6H, m), 2.07-2.40 (4H, m), 3.08 (1H, dd,  
J=13.5, 7 Hz), 3.23-3.46 (2H, m), 3.85 (1H, m), 4.25 (1H, m), 4.32 (2H,  
t, J=6.5 Hz), 4.68 (1H, m), 5.21 (1H, m), 5.89 (1H, s), 7.06 (1H, d,  
20 J=10.3 Hz), 7.41 (2x1H, d, J=8.2 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz),  
7.56 (1H, dddd, J=7.5, 7.5, 1.5, 1.5 Hz), 7.63 (1H, d, J=10.3 Hz),  
7.80 (2x1H, d, J=8.2 Hz), 8.03 (2x1H, dd, J=7.5, 1.5 Hz), 9.97 (1H,  
s);

MASS (ES+): m/e 605.53.

25 Preparation 344

To the Compound (343) (6.50 g) were added a solution of 2-  
methyl-2-butene (4.52 g) in t-butanol (90 ml), a solution of sodium  
hydrogensulfate (1.93 g) in water (20 ml) and sodium chlorite (4.86 g)  
in this order. The mixture was stirred at ambient temperature for 2  
30 hours. To the mixture was added a 5% aqueous solution of potassium  
hydrogensulfide (100 ml) and the mixture was further stirred for 15  
min. The mixture was extracted with chloroform (500 ml) and the  
aqueous layer was further extracted with chloroform (200 ml). The  
organic layers were combined, washed with saturated brine (200 ml),  
35 dried over sodium sulfate and purified by flush chromatography  
(eluting with ethyl acetate 1/1 then 2/1, ethyl acetate, then 10%

methanol in chloroform) to give the objective Compound (344).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.28 (3H, m), 1.36-1.57 (3H, m), 1.60-2.41 (9H, m), 3.06 (1H, dd, J=13.8, 6.5 Hz), 3.21-3.38 (2H, m), 3.78-3.93 (1H, m), 4.21-4.37 (3H, m), 4.69 (1H, brd, J=7.0 Hz), 5.14-5.28 (1H, m), 6.05 (1H, s), 7.13 (1H, d, J=10.3 Hz), 7.34 (2H, d, J=8.0 Hz), 7.45 (2H, d, J=8.0 Hz), 7.52-7.60 (1H, m), 7.65 (1H, d, J=10.3 Hz), 7.96-8.08 (4H, m);  
MASS (ES-): m/e 619.60(M-1).

#### Preparation 345

10 Compound (345) was obtained in a manner similar to Preparation 319.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.36-2.00 (12H, m), 2.05-2.40 (4H, m), 2.98 (1H, dd, J=13.6, 5.9 Hz), 3.19-3.40 (4H, m), 3.57-3.78 (2H, m), 3.80-3.92 (1H, m), 4.19-4.30 (1H, m), 15 4.31 (2H, t, J=6.6 Hz), 4.66 (1H, brd, J=5.9 Hz), 5.19 (1H, dt, J=10.3, 6.2 Hz), 5.90 (1H, s), 7.10 (1H, d, J=10.3 Hz), 7.22-7.36 (4H, m), 7.39-7.49 (2H, m), 7.51-7.65 (2H, m), 7.99-8.08 (2H, m);  
MASS (ES+): m/e 688.59 (M+1).

#### Preparation 346

20 Compound (346) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.22-1.74 (9H, m), 1.29 (3H, s), 2.07-2.41 (4H, m), 2.97 (1H, dd, J=13.6, 5.9 Hz), 3.20-3.39 (4H, m), 3.57-3.76 (2H, m), 3.65 (2H, t, J=6.6 Hz), 3.80-3.92 (1H, 25 m), 4.17-4.30 (1H, m), 4.67 (1H, brd, J=5.9 Hz), 5.19 (1H, dt, J=10.3, 5.9 Hz), 6.02 (1H, s), 7.10 (1H, d, J=10.3 Hz), 7.23-7.34 (4H, m), 7.59 (1H, d, J=9.9 Hz);  
MASS (ES+): m/e 584.56 (M+1).

#### Preparation 347

30 Compound (347) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 187.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.30 (3H, s), 1.41-1.94 (6H, m), 2.08-2.39 (4H, m), 2.50 (2H, brt, J=7.3 Hz), 2.98 (1H, dd, J=13.2, 5.9 Hz), 3.19-3.42 (4H, m), 3.59-3.77 (2H, m), 3.80-3.93 35 (1H, m), 4.17-4.31 (1H, m), 4.67 (1H, brd, J=5.9 Hz), 5.19 (1H, dt, J=9.9, 6.2 Hz), 5.95 (1H, s), 7.11 (1H, d, J=10.3 Hz), 7.23-7.36 (4H,

m), 7.54 (1H, d, J=9.9 Hz), 9.77 (1H, brs);

MASS (ES+): m/e 582.48 (M+1).

#### Preparation 348

5       Compound (348) was obtained in a manner similar to Preparation 303.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>-CD<sub>3</sub>OD (9:1v/v), δ): 0.81 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.34-1.55 (2H, m), 1.61-1.97 (6H, m), 2.03-2.23 (2H, m), 2.25-2.40 (2H, m), 3.06 (1H, dd, J=13.2, 6.6 Hz), 3.22-3.36 (2H, m), 3.75-3.88 (1H, m), 4.23 (1H, t, J=7.5 Hz), 4.32 (2H, t, J=6.2 Hz),  
10 4.72 (1H, brd, J=6.6 Hz), 5.13-5.25 (1H, m), 7.12-7.20 (1H, t, J=7.3 Hz), 7.33-7.49 (5H, m), 7.53-7.61 (1H, m), 7.62-7.69 (2H, m), 7.76-7.86 (3H, m), 7.99-8.06 (1H, m);

MASS (ES+): m/e 696.44 (M+1).

#### Preparation 349

15       Compound (349) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.0 Hz), 1.22-1.94 (8H, m), 1.29 (3H, s), 2.05-2.41 (4H, m), 3.06 (1H, dd, J=13.6, 6.6 Hz), 3.20-3.37 (2H, m), 3.66 (2H, brt, J=6.2 Hz), 3.79-3.93 (1H, m), 4.24 (1H, dq, J=10.3, 7.7 Hz), 4.68 (1H, brd, J=5.5 Hz), 5.15-5.28 (1H, m), 6.00  
20 (1H, s), 7.08 (1H, d, J=10.3 Hz), 7.15 (1H, t, J=7.3 Hz), 7.32-7.44 (4H, m), 7.63 (3H, d, J=8.8 Hz), 7.74-7.85 (3H, m);

MASS (ES+): m/e 592.48 (M+1).

#### Preparation 350

25       Compound (350) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 190.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.30 (3H, s), 1.45-1.95 (6H, m), 2.07-2.40 (4H, m), 2.51 (2H, brt, J=6.6 Hz), 3.05 (1H, dd, J=13.6, 6.2 Hz), 3.23-3.36 (2H, m), 3.81-3.92 (1H, m), 4.17-4.31  
30 (1H, m), 4.68 (1H, brt, J=5.9 Hz), 5.21 (1H, dt, J=9.6, 6.6 Hz), 5.95 (1H, s), 7.09 (1H, d, J=10.3 Hz), 7.16 (1H, t, J=7.5 Hz), 7.33-7.43 (4H, m), 7.58 (1H, d, J=10.3 Hz), 7.63 (1H, t, J=7.7 Hz), 7.74-7.86 (3H, m), 9.78 (1H, brs);

MASS (ES+): m/e 590.48 (M+1).

#### Preparation 351

35       Compound (351) was obtained in a manner similar to Preparation

14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (0.6H, d, J=6.6 Hz), 0.85 (0.6H, d, J=6.6 Hz), 0.92 (2.4H, d, J=6.6 Hz), 0.98 (2.4H, d, J=6.6 Hz), 1.44 (9H, s), 1.86-2.28 (5H, m), 3.50-3.67 (1H, m), 3.82-4.06 (1H, m), 4.35 (1H, dd, J=9.2, 6.2 Hz), 4.49 (1H, dd, J=8.7, 3.6 Hz), 4.96-5.28 (3H, m), 7.30-7.39 (5H, m);

MASS (ES<sup>+</sup>): m/e 405.30 (M+1).

#### Preparation 352

Compound (352) was obtained in a manner similar to Preparation

10 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.73-0.87 (4H, m), 0.92 (2.5H, d, J=6.6 Hz), 0.97 (2.5H, d, J=6.6 Hz), 1.41 (3H, s), 1.43 (9H, s), 1.78-2.26 (7H, m), 3.50-3.64 (1H, m), 3.84-3.95 (1H, m), 4.49 (1H, dd, J=9.2, 3.3 Hz), 4.67 (1H, dd, J=9.2, 6.6 Hz), 4.92-5.22 (3H, m), 6.58-6.75 (1H, m), 7.28-7.40 (5H, m);

MASS (ES<sup>+</sup>): m/e 504.37 (M+1).

#### Preparation 353

Compound (353) was obtained in a manner similar to Preparation

16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.68-0.84 (4H, m), 0.91 (2.5H, d, J=6.6 Hz), 0.96 (2.5H, d, J=6.6 Hz), 1.44 (9H, s), 1.56 (3H, s), 1.66-2.46 (13H, m), 3.51-3.64 (1H, m), 3.81-3.94 (1H, m), 3.98-4.17 (1H, m), 4.32 (2H, brt, J=6.1 Hz), 4.46-4.54 (1H, m), 4.65 (1H, dd, J=9.2, 7.0 Hz), 4.98-5.21 (3H, m), 6.48-6.60 (1H, m), 7.03-7.10 (1H, brs), 7.27-7.65 (8H, m), 8.00-8.07 (2H, m);

MASS (ES<sup>+</sup>): m/e 737.49 (M+1).

#### Preparation 354

Compound (354) was obtained in a manner similar to Preparation

17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 0.95 (6H, d, J=7.0 Hz), 1.44 (9H, s), 1.46 (3H, s), 1.47-3.01 (13H, m), 3.49-3.62 (1H, m), 3.89-4.11 (2H, m), 4.34 (2H, t, J=6.6 Hz), 4.46-4.55 (1H, m), 4.56 (1H, t, J=8.8 Hz), 5.30-5.45 (1H, m), 6.88-6.97 (1H, m), 7.06-7.16 (1H, m), 7.40-7.48 (2H, m), 7.52-7.60 (1H, m), 8.01-8.07 (2H, m);

MASS (ES<sup>+</sup>): m/e 647.31 (M+1).

#### Preparation 355

Compound (355) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78-0.98 (9H, m), 1.42 (3H, s), 1.46-2.23 (13H, m), 3.44-3.60 (1H, m), 3.88-4.01 (1H, m), 4.17-4.39 (4H, m),  
5 4.44-4.57 (1H, m), 7.36-7.58 (3H, m), 8.01 (2H, d, J=7.3 Hz), 8.04-8.37 (4H, m);

MASS (ES+): m/e 547.34 (free, M+1).

#### Preparation 356

Compound (356) was obtained in a manner similar to Preparation 10 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 0.91 (3H, d, J=6.6 Hz), 0.98 (3H, d, J=6.6 Hz), 1.29 (3H, s), 1.36-2.01 (8H, m), 2.11-2.44 (5H, m), 3.47-3.60 (1H, m), 3.83-3.95 (1H, m), 4.19-4.29 (1H, m),  
15 4.31 (2H, t, J=6.6 Hz), 4.48 (1H, t, J=10.3 Hz), 4.75 (1H, brd, J=7.7 Hz), 5.79 (1H, s), 7.16 (1H, d, J=10.6 Hz), 7.38 (1H, d, J=10.6 Hz), 7.40-7.48 (2H, m), 7.52-7.60 (1H, m), 8.00-8.06 (2H, m);

MASS (ES+): m/e 529.48 (M+1).

#### Preparation 357

Compound (357) was obtained in a manner similar to Preparation 20 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.88 (3H, t, J=7.3 Hz), 0.91 (3H, d, J=6.2 Hz), 0.98 (3H, d, J=6.6 Hz), 1.23-1.71 (5H, m), 1.30 (3H, s), 1.76-2.02 (3H, m), 2.12-2.44 (5H, m), 3.47-3.58 (1H, m), 3.60-3.70 (2H, m),  
25 3.83-3.95 (1H, m), 4.23 (1H, dt, J=10.3, 7.7 Hz), 4.48 (1H, t, J=10.3 Hz), 4.75 (1H, brd, J=8.1 Hz), 5.94 (1H, s), 7.17 (1H, d, J=10.3 Hz), 7.39 (1H, d, J=10.6 Hz);

MASS (ES+): m/e 425.36 (M+1).

#### Preparation 358

Compound (358) was obtained in a manner similar to Preparation 30 78. The obtained compound was used in Example 193.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.88 (3H, t, J=7.3 Hz), 0.90 (3H, d, J=6.6 Hz), 0.99 (3H, d, J=7.0 Hz), 1.31 (3H, s), 1.48-1.75 (5H, m), 1.75-2.02 (3H, m), 2.11-2.45 (5H, m), 2.49 (2H, brt, J=7.3 Hz), 3.53 (1H, dt, J=10.3, 7.3 Hz), 3.84-3.95 (1H, m), 4.17-4.28 (1H, m), 4.47 (1H, t, J=10.3 Hz),  
35 4.75 (1H, dd, J=7.7, 1.8 Hz), 5.85 (1H, s), 7.17 (1H, d, J=10.6 Hz), 7.32 (1H, d, J=10.6 Hz), 9.77 (1H, t, J=1.5 Hz);

MASS (ES+): m/e 423.36 (M+1).

Preparation 359

Compound (359) was obtained in a manner similar to Preparation 13.

- 5  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.42 (9H, s), 2.97-3.26 (2H, m), 3.87 (3H, s), 4.53-4.65 (1H, m), 4.96 (1H, brd,  $J=7.0$  Hz), 6.68-6.77 (2H, m), 7.28 (1H, d,  $J=8.8$  Hz);

MASS (ES-): m/e 328.19(M-1).

Preparation 360

- 10 Compound (360) was obtained in a manner similar to Preparation 14.

- $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.43 (9H, s), 1.54-1.68 (1H, m), 1.84-2.07 (3H, m), 2.69-2.84 (1H, m), 2.88-3.07 (2H, m), 3.52-3.66 (1H, m), 3.85 (0.5H, s), 3.87 (2.5H, s), 4.36 (1H, dd,  $J=8.1$ , 4.4 Hz), 4.58-4.73 (1H, m),  
15 m), 5.03-5.25 (2H, m), 5.34 (1H, d,  $J=8.4$  Hz), 6.69-6.80 (2H, m), 7.17-7.40 (6H, m);

MASS (ES+): m/e 517.29 (M+1).

Preparation 361

- 20 Compound (361) was obtained in a manner similar to Preparation 15.

- $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.81 (3H, t,  $J=7.7$  Hz), 1.39 (3H, s), 1.43 (9H, s), 1.53-1.72 (1H, m), 1.77-2.05 (5H, m), 2.74-2.88 (1H, m), 2.89-3.08 (2H, m), 3.50-3.65 (1H, m), 3.84 (0.5H, s), 3.88 (2.5H, s), 4.38 (1H, dd,  $J=8.1$ , 3.8 Hz), 4.73-5.20 (3H, m), 6.55-6.93 (3H, m),  
25 7.14-7.40 (6H, m);

MASS (ES+): m/e 616.38 (M+1).

Preparation 362

Compound (362) was obtained in a manner similar to Preparation 16.

- 30  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.63 (0.5H, t,  $J=7.7$  Hz), 0.74 (2.5H, t,  $J=7.7$  Hz), 1.30-2.33 (12H, m), 1.41 (9H, s), 1.47 (3H, s), 2.75-3.09 (3H, m), 3.53-3.70 (1H, m), 3.83 (0.5H, s), 3.86 (2.5H, s), 4.00-4.15 (1H, m), 4.26-4.44 (3H, m), 4.88-5.05 (1H, m), 5.07-5.22 (2H, m), 6.55-6.96 (4H, m), 7.14-7.65 (10H, m), 7.99-8.07 (2H, m);

- 35 MASS (ES+): m/e 849.51 (M+1).

Preparation 363

Compound (363) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.76 (3H, t, J=7.7 Hz), 1.42-2.25 (12H, m), 1.43 (3H, s), 1.44 (9H, s), 2.75-3.45 (3H, m), 3.61-3.81 (1H, m), 3.88 (3H, s), 3.92-4.07 (1H, m), 4.25-4.43 (3H, m), 4.86-5.05 (1H, m), 6.67-6.95 (3H, m), 7.15-7.27 (2H, m), 7.29-7.37 (1H, m), 7.39-7.48 (2H, m), 7.52-7.63 (1H, m), 7.97-8.07 (2H, m);

MASS (ES+): m/e 759.54 (M+1).

#### Preparation 364

Compound (364) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.65-0.80 (3H, m), 1.27-2.37 (12H, m), 1.39 (3H, brs), 2.78-3.20 (3H, m), 3.68-3.93 (3H, m), 3.86 (3H, brs), 4.16-4.43 (3H, m), 4.95 (1H, brs), 6.68-6.77 (1H, m), 6.84 (1H, brs), 7.16-7.24 (1H, m), 7.35-7.45 (2H, m), 7.49-7.58 (1H, m), 7.65-7.75 (1H, m), 7.95-8.03 (2H, m), 8.10-8.30 (3H, m);

MASS (ES+): m/e 659.50 (M+1, free).

#### Preparation 365

Compound (365) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.30-2.00 (8H, m), 2.02-2.40 (4H, m), 2.94 (1H, dd, J=13.6, 6.2 Hz), 3.16-3.34 (3H, m), 3.79-3.90 (1H, m), 3.87 (3H, s), 4.19-4.31 (1H, m), 4.32 (2H, t, J=6.6 Hz), 4.64-4.71 (1H, m), 5.17 (1H, dt, J=9.9, 6.2 Hz), 5.88 (1H, brs), 6.77 (1H, dd, J=7.7, 1.5 Hz), 6.80-6.84 (1H, m), 7.09 (1H, d, J=10.3 Hz), 7.25 (1H, d, J=7.3 Hz), 7.39-7.48 (2H, m), 7.52-7.63 (2H, m), 8.00-8.06 (2H, m);

MASS (ES+): m/e 641.50 (M+1).

#### Preparation 366

Compound (366) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.21-1.94 (8H, m), 1.29 (3H, s), 2.07-2.40 (4H, m), 2.94 (1H, dd, J=13.6, 6.2 Hz), 3.21 (1H, dd, J=13.6, 9.5 Hz), 3.23-3.24 (1H, m), 3.60-3.70 (2H, m), 3.80-3.90 (1H, m), 3.87 (3H, s), 4.18-4.30 (1H, m), 4.68 (1H, brd, J=5.9 Hz), 5.17 (1H, dt, J=10.3, 6.2 Hz), 6.01 (1H, brs), 6.77 (1H, dd,

J=8.1, 1.8 Hz), 6.82 (1H, brs), 7.09 (1H, d, J=9.9 Hz), 7.25 (1H, d, J=7.7 Hz), 7.60 (1H, d, J=9.9 Hz);

MASS (ES+): m/e 537.46 (M+1).

Preparation 367

5           Compound (367) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 196.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.7 Hz), 1.29 (3H, s), 1.47-1.95 (6H, m), 2.07-2.41 (4H, m), 2.50 (2H, brt, J=7.0 Hz), 2.94 (1H, dd, J=13.6, 6.2 Hz), 3.20 (1H, dd, J=13.6, 9.5 Hz), 3.21-3.34 (1H, m),  
10 3.79-3.92 (1H, m), 3.87 (3H, s), 4.18-4.30 (1H, m), 4.68 (1H, brd, J=5.9 Hz), 5.16 (1H, dt, J=9.9, 6.2 Hz), 5.92 (1H, brs), 6.77 (1H, dd, J=8.1, 1.8 Hz), 6.81 (1H, brs), 7.10 (1H, d, J=10.3 Hz), 7.25 (1H, d, J=8.1 Hz), 7.54 (1H, d, J=10.3 Hz), 9.77 (1H, s);

MASS (ES+): m/e 535.43 (M+1).

15       Preparation 368

Compound (368) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.33 (2H, s), 1.42 (7H, s), 1.53-1.69 (1H, m), 1.78-2.06 (3H, m), 2.68-2.84 (1H, m), 2.89-3.08 (2H, m), 3.52-3.66  
20 (1H, m), 4.39 (1H, dd, J=7.7, 4.0 Hz), 4.58-4.69 (1H, m), 5.10 (1H, d, J=12.5 Hz), 5.20 (1H, d, J=12.5 Hz), 5.35 (1H, brd, J=8.8 Hz), 6.78-6.96 (3H, m), 7.00 (1H, brd, J=7.7 Hz), 7.13-7.28 (2H, m), 7.28-7.42 (4H, m);

MASS (ES+): m/e 471.25 (M+1).

25       Preparation 369

Compound (369) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.7 Hz), 1.38 (3H, s), 1.39 (2H, s), 1.49 (7H, s), 1.54-1.70 (1H, m), 1.76-2.08 (5H, m), 2.72-2.90  
30 (1H, m), 2.97 (1H, dd, J=13.2, 8.8 Hz), 3.05 (1H, dd, J=13.2, 5.1 Hz), 3.47-3.67 (1H, m), 4.40 (1H, dd, J=8.4, 4.0 Hz), 4.94 (1H, dt, J=8.8, 5.4 Hz), 4.99-5.25 (3H, m), 6.64-7.04 (4H, m), 7.11-7.26 (2H, m), 7.27-7.40 (4H, m);

MASS (ES+): m/e 570.44 (M+1).

35       Preparation 370

Compound (370) was obtained in a manner similar to Preparation

16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60 (0.6H, t, J=7.2 Hz), 0.73 (2.4H, t, J=7.2 Hz), 1.35-2.34 (12H, m), 1.44 (3H, s), 1.48 (9H, s), 2.76-3.12 (3H, m), 3.51-3.70 (1H, m), 3.90-4.16 (1H, m), 4.31 (2H, t, J=7.0 Hz),  
5 4.42 (1H, dd, J=8.2, 4.0 Hz), 4.98-5.02 (1H, m), 5.04-5.25 (2H, m),  
6.69-7.03 (5H, m), 7.08-7.66 (10H, m), 7.99-8.08 (2H, m);

MASS (ES<sup>+</sup>): m/e 803.40 (M+1).

Preparation 371

Compound (371) was obtained in a manner similar to Preparation

10 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.3 Hz), 1.37-2.25 (12H, m),  
1.43 (3H, s), 1.45 (9H, s), 2.82-3.16 (3H, m), 3.65-3.80 (1H, m),  
3.93-4.08 (1H, m), 4.25-4.45 (3H, m), 4.89-5.02 (1H, m), 5.30 (1H,  
brs), 6.82 (1H, brs), 6.88-7.06 (3H, m), 7.20-7.30 (1H, m), 7.33 (1H,  
15 brd, J=10.3 Hz), 7.39-7.49 (2H, m), 7.52-7.62 (1H, m), 7.99-8.08 (2H,  
m);

MASS (ES<sup>+</sup>): m/e 711.23(M-1).

Preparation 372

Compound (372) was obtained in a manner similar to Preparation

20 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.33-  
1.57 (2H, m), 1.61-1.96 (6H, m), 2.07-2.37 (4H, m), 2.98 (1H, dd,  
J=13.6, 6.2 Hz), 3.06-3.35 (2H, m), 3.81 (1H, dt, J=9.2, 4.4 Hz),  
4.18-4.28 (1H, m), 4.32 (2H, t, J=6.2 Hz), 4.73 (1H, brd, J=7.7 Hz),  
25 5.09-5.20 (1H, m), 6.85-7.05 (4H, m), 7.20-7.35 (2H, m), 7.41-7.49 (2H,  
m), 7.54-7.61 (1H, m), 7.76 (1H, d, J=10.3 Hz), 7.99-8.06 (2H, m).

Preparation 373

Compound (373) was obtained in a manner similar to Preparation

77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.23-1.71 (6H, m),  
1.29 (3H, s), 1.73-1.96 (2H, m), 2.08-2.42 (4H, m), 2.97 (1H, dd,  
J=13.6, 6.2 Hz), 3.23 (1H, dd, J=13.6, 9.5 Hz), 3.27-3.36 (1H, m),  
3.61-3.71 (2H, m), 3.81-3.92 (1H, m), 4.24 (1H, dt, J=10.3, 7.3 Hz),  
4.70 (1H, brd, J=5.5 Hz), 5.17 (1H, dt, J=9.5, 6.6 Hz), 5.98 (1H, s),  
35 6.87-6.99 (2H, m), 7.02 (1H, d, J=7.7 Hz), 7.10 (1H, d, J=10.3 Hz),  
7.20-7.32 (1H, m), 7.59 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 491.32 (M+1).

Preparation 374

Compound (374) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 199.

5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.7 Hz), 1.29 (3H, s), 1.50-1.93 (4H, m), 2.09-2.40 (6H, m), 2.51 (2H, brt, J=6.3 Hz), 2.97 (1H, dd, J=13.6, 6.6 Hz), 3.22 (1H, dd, J=13.6, 9.2 Hz), 3.24-3.36 (1H, m), 3.81-3.92 (1H, m), 4.24 (1H, dt, J=10.3, 7.3 Hz), 4.65-4.72 (1H, m), 5.16 (1H, dt, J=10.3, 6.6 Hz), 5.88 (1H, brs), 6.86-6.98 (2H, m), 7.01  
10 (1H, d, J=10.3 Hz), 7.10 (1H, d, J=10.3 Hz), 7.19-7.29 (1H, m), 7.52 (1H, d, J=10.3 Hz), 9.77 (1H, t, J=1.5 Hz);

MASS (ES+): m/e 489.23 (M+1).

Preparation 375

To a stirred solution of ethyl R-mandelate (7.0 g) in N,N-  
15 dimethylformamide (70 mL) was added imidazole (2.91 g) followed by tert-butyldiphenylchlorosilane (10.7 g) at ambient temperature and the resulting mixture was stirred at the same temperature for two hours. To this mixture was added additional tert-butyldiphenylchlorosilane (1.07 g) and imidazole (530 mg) and the mixture was stirred at ambient  
20 temperature for sixteen hours. The reaction mixture was poured into water and

extracted with ethyl acetate. The organic layer was successively washed with water, 0.2 N hydrochloric acid, saturated aqueous sodium bicarbonate solution and brine. The organic layer was dried over  
25 magnesium sulfate, filtered and evaporated to give Compound (375) (17.4 g) as a pale yellow oil, which was used in the next step without further purification.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.05 (3H, t, J=7.3 Hz), 1.11 (9H, s), 3.85-3.92 (2H, m), 5.13 (1H, s), 7.14-7.54 (11H, m), 7.69-7.76 (4H, m).

30 Preparation 376

Compound (376) was obtained in a manner similar to Preparation 117.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.11 (9H, s), 2.92 (1H, dd, J=21.6, 15.8 Hz), 3.18 (1H, dd, J=20.1, 15.8 Hz), 3.49 (3H, d, J=11.4 Hz), 3.59 (3H,  
35 d, J=11.4 Hz), 5.21 (1H, s), 7.21-7.49 (13H, m), 7.62-7.68 (2H, m);

MASS (ES+): m/e 519.10(M+Na).

Preparation 377

Compound (377) was obtained in a manner similar to Preparation 14.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.32 (9x1/6H, s), 1.41 (9x5/6H, s), 1.68 (1H, m), 1.84-2.32 (3H, m), 2.73 (1x1/6H, dd, J=14, 10 Hz), 2.91-3.06 (3x5/6H, m), 3.64 (1H, m), 4.39 (1H, dd, J=8, 4 Hz), 4.69 (1H, brdt, J=8, 7 Hz), 5.11 (1H, d, J=12 Hz), 5.21 (1H, d, J=12 Hz), 5.31 (1H, d, J=8 Hz), 6.97 (2x1/6H, d, J=6 Hz), 7.16 (2x5/6H, d, J=6 Hz), 7.29-7.41 (5H, m), 8.43 (2x1/6H, d, J=6 Hz), 8.50 (2x5/6H, d, J=6 Hz);
- 10 MASS (ES+): m/e 454.41.

Preparation 378

Compound (378) was obtained in a manner similar to Preparation 15.

- <sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.84-1.98 (3H, m), 2.18 (1H, m), 3.30 (1H, dd, J=14, 7.5 Hz), 3.40-3.58 (2H, m), 3.84 (1H, m), 4.41 (1H, dd, J=8.5, 2.5 Hz), 4.72 (1H, br), 5.09 (1H, d, J=12.5 Hz), 5.19 (1H, d, J=12.5 Hz), 7.30-7.44 (5H, m), 7.78 (2x1/6H, d, J=6.5 Hz), 7.91 (2x5/6H, d, J=6.5 Hz), 8.56 (2x5/6H, br), 8.64 (2x1/6H, br), 8.84 (2H, d, J=6.5 Hz);
- 20 MASS (ES+): m/e 354.25.

Preparation 379

Compound (379) was obtained in a manner similar to Preparation 15.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.57 (3x1/4H, t, J=7.5 Hz), 0.80 (3x3/4H, t, J=7.5 Hz), 1.31 (3/1/4H, s), 1.37 (9x1/4H, s), 1.39 (3x3/4H, s), 1.43 (9x3/4H, s), 1.65-2.35 (6H, m), 2.86 (1x1/4H, dd, J=14, 9.5 Hz), 2.96-3.24 (3x3/4H, m), 3.72 (1H, m), 4.41 (1x3/4H, dd, J=8, 3.5 Hz), 4.75-5.22 (4x1/4H, m), 6.74 (1x1/4H, d, J=8.5 Hz), 6.91 (1x3/4H, d, J=8.5 Hz), 7.01 (2x1/4H, d, J=6 Hz), 7.22 (2x3/4H, d, J=6 Hz), 7.29-7.42 (5H, m), 8.40 (2x1/4H, d, J=6 Hz), 8.50 (2x3/4H, d, J=6 Hz);
- 30 MASS (ES+): m/e 553.30.

Preparation 380

Compound (380) was obtained in a manner similar to Preparation 16.

- <sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 0.72 (3x1/6H, t, J=7.3 Hz), 0.76 (3x5/6H, t, J=7.3 Hz), 1.27 (3H, s), 1.62-2.31 (6H, m), 3.05-3.82 (4H, m), 4.41

(1H, dd, J=8, 4 Hz), 5.03 (1H, d, J=12, 5 Hz), 5.07 (1H, m), 5.18 (1H, d, J=12.5 Hz), 7.30-7.42 (5H, m), 7.57 (2x1/6H, d, J=6 Hz), 7.87 (2x5/6H, d, J=6 Hz), 8.04 (2x5/6H, s), 8.13 (2x1/6H, s), 8.69-9.00 (3H, m);

5 MASS (ES+): m/e 453.24.

Preparation 381

Compound (381) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.63 (1x3/4H, t, J=7 Hz), 0.75 (3x3/4H, t, J=7 Hz), 1.32-2.32 (24H, m), 2.90-3.23 (3H, m), 3.53-4.47 (5H, m), 4.92-5.21 (4H, m), 6.82-6.98 (2H, m), 7.04 (2x1/4H, d, J=6 Hz), 7.22 (2x3/4H, d, J=6 Hz), 7.24-7.38 (5H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, dd, J=7.5, 7.5 Hz), 8.03 (2x1H, d, J=7.5 Hz), 8.41 (2x1/4H, d, J=6 Hz), 8.50 (2x3/4H, d, J=6 Hz);

15 MASS (ES+): m/e 786.26.

Preparation 382

Compound (382) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.62-0.86 (3H, m), 1.26-2.32 (24H, m), 3.04-3.85 (4H, m), 3.90-5.58 (7H, m), 7.37-7.49 (2H, m), 7.55 (1H, m), 7.85-8.10 (4H, m), 8.67 (2H, br);

MASS (ES+): m/e 696.29.

Preparation 383

Compound (383) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.67 (3H, m), 1.22-2.28 (15H, m), 3.04-3.76 (4H, m), 4.21-4.44 (2H, m), 4.60-5.40 (3H, m), 7.41 (2x1H, brdd, J=7, 7 Hz), 7.55 (1H, brdd, J=7, 7 Hz), 7.66-8.04 (6H, m), 8.67 (2H, br);

MASS (ES-): m/e 594.39.

30 Preparation 384

Compound (384) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.4 Hz), 1.28 (3H, s), 1.38-1.58 (2H, m), 1.62-1.98 (6H, m), 2.07-2.40 (4H, m), 3.02 (1H, m), 3.22 (1H, dd, J=14, 9 Hz), 3.36 (1H, m), 3.86 (1H, m), 4.26 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.69 (1H, m), 5.21 (1H, m), 5.84 (1H, s), 7.02 (1H,

d, J=10 Hz), 7.19 (2x1H, d, J=5.5 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 7.63 (1H, d, J=10 Hz), 8.03 (2x1H, brd, J=7.5 Hz), 8.52 (2x1H, d, J=5.5 Hz);

MASS (ES+): m/e 578.31.

5 Preparation 385

Compound (385) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.20-1.94 (8H, m), 1.28 (3H, s), 2.04-2.42 (4H, m), 3.01 (1H, dd, J=14, 7 Hz), 3.21 (1H, dd, J=14, 8.7 Hz), 3.34 (1H, m), 3.66 (2H, t, J=6.2 Hz), 3.86 (1H, m), 4.24 (1H, dt, J=10.2, 7.7 Hz), 4.69 (1H, m), 5.21 (1H, ddd, J=10.2, 8.7, 7 Hz), 6.00 (1H, s), 7.03 (1H, d, J=10.2 Hz), 7.18 (2x1H, d, J=4.5 Hz), 7.64 (1H, d, J=10.2 Hz), 8.51 (2x1H, d, J=4.5 Hz);

MASS (ES+): m/e 474.36.

15 Preparation 386

Compound (386) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 208.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.50-1.94 (6H, m), 2.08-2.40 (4H, m), 2.51 (2H, m), 3.01 (1H, dd, J=14, 7 Hz), 3.21 (1H, dd, J=14, 8.5 Hz), 3.34 (1H, m), 3.86 (1H, m), 4.24 (1H, m), 4.69 (1H, m), 5.21 (1H, ddd, J=10, 8.5, 7 Hz), 5.88 (1H, s), 7.03 (1H, d, J=10 Hz), 7.17 (2x1H, d, J=6 Hz), 7.58 (1H, d, J=10 Hz), 8.51 (2x1H, d, J=6 Hz), 9.77 (1H, s);

MASS (ES+): m/e 472.35.

25 Preparation 387

Compound (387) was obtained in a manner similar to Preparation 311.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.36-1.98 (8H, m), 2.06-2.40 (4H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.24 (1H, dt, J=10, 7.5 Hz), 4.32 (2H, t, J=6.5 Hz), 4.50 (2H, brd, J=5 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.28 (1H, brd, J=10.5 Hz), 5.40 (1H, brd, J=17 Hz), 5.79 (1H, s), 6.04 (1H, ddt, J=17, 10.5, 5 Hz), 6.83 (2x1H, d, J=8.5 Hz), 7.09-7.20 (3H, m), 7.44 (2x1H, dd, J=8, 8 Hz), 7.52 (1H, d, J=10 Hz), 7.54 (1H, m), 8.03 (2x1H, brd, J=8 Hz);

MASS (ES+): m/e 633.32.

Preparation 388

Compound (388) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.48 (3H, m),  
5 1.57-1.92 (5H, m), 2.09-2.42 (4H, m), 2.89 (1H, dd, J=14, 6 Hz), 3.18  
(1H, dd, J=14, 10 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.05 (2H, t, J=6.5  
Hz), 4.21 (1H, m), 4.50 (2H, m), 4.67 (1H, dd, J=8, 2 Hz), 5.13 (1H,  
ddd, J=10.5, 10, 6 Hz), 5.28 (1H, dd, J=10, 1.5 Hz), 5.40 (1H, dd,  
J=17, 1.5 Hz), 5.81 (1H, s), 6.04 (1H, m), 6.82 (2x1H, d, J=8.5 Hz),  
10 7.13 (1H, d, J=10 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.52 (1H, d, J=10.5  
Hz);

MASS (ES<sup>+</sup>): m/e 571.36.

Preparation 389

Compound (389) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.94 (9H, m),  
1.28 (3H, s), 2.08-2.41 (4H, m), 2.87 (1H, dd, J=13.5, 6 Hz), 3.18 (1H,  
dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.65 (2H, br), 3.85 (1H, m), 4.23  
(1H, m), 4.50 (2H, m), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz),  
20 5.28 (1H, dd, J=10.5, 2 Hz), 5.41 (1H, dd, J=17.5, 2 Hz), 5.89 (1H, s),  
6.04 (1H, m), 6.82 (2x1H, d, J=8.5 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.14  
(1H, d, J=10 Hz), 7.52 (1H, d, J=10 Hz);

MASS (ES<sup>+</sup>): m/e 529.37.

Preparation 390

Compound (390) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 211.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3x3H, s),  
1.48-1.92 (6H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 2.88 (1H, dd,  
J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.24 (1H, m), 3.86 (1H,  
30 m), 4.22 (1H, m), 4.49 (2H, ddd, J=5, 1.5, 1.5 Hz), 4.66 (1H, m), 5.13  
(1H, ddd, J=10, 10, 6 Hz), 5.17 (1H, ddt, J=10.5, 1.5, 1.5 Hz), 5.40  
(1H, ddt, J=17, 1.5, 1.5 Hz), 5.83 (1H, s), 6.04 (1H, ddt, J=17, 10.5,  
5 Hz), 6.82 (2x1H, d, J=8.5 Hz), 7.13 (2x1H, d, J=8.5 Hz), 7.14 (1H, d,  
J=10 Hz), 7.46 (1H, d, J=10 Hz), 9.77 (1H, s);

35 MASS (ES<sup>+</sup>): m/e 527.40.

Preparation 391

Compound (391) was obtained in a manner similar to Preparation 311.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.31 (2x3H, d, J=6 Hz), 1.38-1.55 (2H, m), 1.58-2.00 (6H, m), 2.06-2.40 (4H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.24 (1H, dt, J=10, 7.7 Hz), 4.31 (2H, t, J=6.5 Hz), 4.49 (1H, qq, J=6, 6 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.14 (1H, ddd, J=10, 10, 6 Hz), 5.80 (1H, s), 6.79 (2x1H, d, J=8.8 Hz), 7.12 (2x1H, d, J=8.8 Hz), 7.14 (1H, d, J=10 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, d, J=10 Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);  
MASS (ES<sup>+</sup>): m/e 635.29.

#### Preparation 392

Compound (392) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.31 (2x3H, d, J=6.3 Hz), 1.34-1.94 (8H, m), 2.08-2.39 (4H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.66 (2H, t, J=6.2 Hz), 3.86 (1H, m), 4.22 (1H, dt, J=10, 7.5 Hz), 4.49 (1H, qq, J=6.3, 6.3 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.14 (1H, ddd, J=10, 9.5, 6 Hz), 5.89 (1H, s), 6.79 (2x1H, d, J=8.5 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.14 (1H, d, J=10 Hz), 7.51 (1H, d, J=10 Hz);  
MASS (ES<sup>+</sup>): m/e 531.46.

#### Preparation 393

Compound (393) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 214.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.4 Hz), 1.29 (3H, s), 1.31 (3H, d, J=6.5 Hz), 1.49-1.91 (6H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.22 (1H, dt, J=10, 7.5 Hz), 4.49 (1H, qq, J=6.5, 6.5 Hz), 4.67 (1H, dd, J=8, 2.5 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.83 (1H, s), 6.79 (2x1H, d, J=9 Hz), 7.12 (2x1H, d, J=9 Hz), 7.15 (1H, d, J=10 Hz), 7.44 (1H, d, J=10 Hz), 9.77 (1H, t, J=1.5 Hz);  
MASS (ES<sup>+</sup>): m/e 529.38.

#### Preparation 394

Compound (394) was obtained in a manner similar to Preparation 311.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.38-1.98 (11H, m), 2.08-2.40 (4H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (1H, m), 4.24 (1H, dt, J=10, 7.5 Hz), 4.31 (2H, t, J=6.5 Hz), 4.41 (2x4/5H, brd, J=6 Hz),
- 5 4.55 (2x1/5H, brd, J=6 Hz), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.65-5.91 (2H, m), 5.80 (1H, s), 6.81 (2x1H, d, J=8.7 Hz), 7.13 (2x1H, d, J=8.7 Hz), 7.14 (1H, d, J=10 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, d, J=10 Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);
- 10 MASS (ES<sup>+</sup>): m/e 647.39.

#### Preparation 395

Compound (395) was obtained in a manner similar to Example 3 mentioned below.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 0.96 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.36-1.55 (4H, m), 1.57-1.98 (8H, m), 2.06-2.40 (4H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.86 (1H, m), 3.92 (2H, t, J=6.5 Hz), 4.24 (1H, dt, J=10, 7.5 Hz), 4.31 (2H, t, J=6.5 Hz), 4.66 (1H, dd, J=8, 2 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.79 (1H, s), 6.80 (2x1H, d, J=8.8 Hz), 7.12 (2x1H, d, J=8.8 Hz), 7.14 (1H, d, J=10 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, d, J=10 Hz), 7.56 (1H, m), 8.03 (1H, dd, J=7.5, 1.5 Hz);
- 20 MASS (ES<sup>+</sup>): m/e 649.41.

#### Preparation 396

- Compound (396) was obtained in a manner similar to Preparation
- 25 77.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 0.96 (3H, t, J=7.3 Hz), 1.24-1.93 (12H, m), 1.28 (3H, s), 2.08-2.40 (4H, m), 2.88 (1H, dd, J=13.5, 5.5 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.65 (2H, brt, J=6.2 Hz), 3.86 (1H, m), 3.91 (2H, t, J=6.5 Hz), 4.22 (1H, dt, J=10, 7.5 Hz), 4.67 (1H, dd, J=8, 2.5 Hz), 5.13 (1H, ddd, J=10, 10, 5.5 Hz), 5.88 (1H, s), 6.80 (2x1H, d, J=8.5 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.13 (1H, d, J=10 Hz), 7.51 (1H, d, J=10 Hz);
- 30 MASS (ES<sup>+</sup>): m/e 545.35.

#### Preparation 397

- Compound (397) was obtained in a manner similar to Preparation
- 35 78. The obtained compound was used in Example 217.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 0.96 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.40-1.92 (10H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 2.88 (1H, dd, J=13.8, 6 Hz), 3.17 (1H, dd, J=13.8, 10 Hz), 3.25 (1H, m), 3.86 (1H, m), 3.92 (2H, t, J=6.5 Hz), 4.23 (1H, m), 4.67 (1H, dd, J=8, 2 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.83 (1H, s), 6.80 (2x1H, d, J=8.5 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.15 (1H, d, J=10 Hz), 7.46 (1H, d, J=10 Hz), 9.77 (1H, s);

MASS (ES+): m/e 543.41.

#### Preparation 398

10 Compound (398) was obtained in a manner similar to Preparation 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.89 (3H, t, J=7.5 Hz), 1.45 (3x3H, s), 1.53 (3H, s), 1.81-1.96 (2H, m), 5.18 (1H, brs);

MASS (ES+): m/e 218.27.

#### Preparation 399

Compound (399) was obtained in a manner similar to Preparation 15.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.5 Hz), 1.22-2.00 (6H, m), 1.45 (3x3H, s), 1.48 (3H, s), 2.59 (1H, m), 2.91 (1H, dd, J=12.8, 10 Hz), 3.11 (1H, dd, J=12.8, 5 Hz), 3.50 (1H, m), 4.36 (1H, dd, J=8, 4 Hz), 4.94 (1H, ddd, J=10, 8, 5 Hz), 5.11 (1H, d, J=12.5 Hz), 5.16 (1H, d, J=12.5 Hz), 5.16 (1H, s), 6.81 (1H, d, J=8 Hz), 7.16-7.42 (10H, m);

MASS (ES+): m/e 552.36.

#### Preparation 400

25 Compound (400) was obtained in a manner similar to Preparation 16.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.65 (3x1/3H, t, J=7.3 Hz), 0.98 (3x2/3H, t, J=7.3 Hz), 1.43-2.40 (6H, m), 1.56 (3x1/3H, s), 1.67 (3x2/3H, s), 2.64 (1H, m), 2.98-3.24 (2H, m), 3.60 (1H, m), 4.33 (1H, m), 4.75 (1x1/3H, m), 4.91 (1x2/3H, m), 5.08-5.26 (2H, m), 7.12-7.42 (10+2/3H, m), 7.89 (1x1/3H, d, J=8 Hz), 8.60-8.92 (2H, m);

MASS (ES+): m/e 452.40.

#### Preparation 401

35 Compound (401) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, t, J=7.3 Hz), 1.38-1.98 (11H, m),

1.44 (3x3H, s), 1.52 (3H, s), 2.29 (1H, m), 2.66 (1H, m), 2.93 (1H, dd, J=13, 9 Hz), 3.07 (1H, dd, J=13, 5.5 Hz), 3.52 (1H, m), 4.08 (1H, m), 4.26-4.42 (3H, m), 4.92 (1H, ddd, J=9, 8, 5.5 Hz), 5.10 (1H, d, J=12 Hz), 5.13 (1H, m), 5.16 (1H, d, J=12 Hz), 6.69 (1H, d, J=8 Hz), 7.01 (1H, s), 7.02-7.40 (10H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES+): m/e 785.36.

#### Preparation 402

Compound (402) was obtained in a manner similar to Preparation

10 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.5 Hz), 1.36-2.04 (11H, m), 1.45 (3x3H, s), 1.48 (3H, s), 2.20 (1H, m), 2.64 (1H, m), 2.88-3.13 (2H, m), 3.64 (1H, m), 4.00 (1H, m), 4.26-4.40 (3H, m), 4.88 (1H, m), 5.19 (1H, m), 6.79 (1H, brs), 7.18-7.36 (6H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.04 (2x1H, d, J=7.5 Hz);

MASS (ES+): m/e 695.35.

#### Preparation 403

Compound (403) was obtained in a manner similar to Preparation

18.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.53-0.90 (3H, m), 1.35-2.16 (12H, m), 1.46 (3H, s), 2.83-3.19 (3H, m), 3.70 (1H, m), 4.10-4.59 (4H, m), 4.88 (1H, m), 7.10-7.32 (6H, m), 7.40 (2x1H, dd, J=7.5, 7.5 Hz), 7.53 (1H, dd, J=7.5, 7.5 Hz), 8.00 (2x1H, d, J=7.5 Hz), 8.11-8.54 (2H, m);

MASS (ES+): m/e 595.39.

25 Preparation 404

Compound (404) was obtained in a manner similar to Preparation

76.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.94 (3H, t, J=7.3 Hz), 1.37-1.59 (2H, m), 1.61-1.97 (8H, m), 1.73 (3H, s), 2.16 (1H, m), 2.30 (1H, m), 2.95 (1H, dd, J=13.5, 5.5 Hz), 3.20 (1H, m), 3.28 (1H, dd, J=13.5, 10 Hz), 3.88 (1H, m), 4.24 (1H, dt, J=10, 7.5 Hz), 4.32 (2H, t, J=6.3 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.16 (1H, ddd, J=10, 10, 5 Hz), 5.86 (1H, s), 7.15 (1H, d, J=10 Hz), 7.16-7.33 (5H, m), 7.40-7.50 (3H, m), 7.56 (1H, m), 8.03 (2x1H, d, J=7.5 Hz);

35 MASS (ES-): m/e 575.46.

#### Preparation 405

Compound (405) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.95 (3H, t, J=7.5 Hz), 1.29-1.93 (10H, m), 1.73 (3H, s), 2.13 (1H, m), 2.30 (1H, m), 2.95 (1H, dd, J=13.5, 5.5 Hz), 3.20 (1H, m), 3.27 (1H, dd, J=13.5, 10 Hz), 3.66 (2H, t, J=6.5 Hz), 3.88 (1H, m), 4.23 (1H, dt, J=10, 7.5 Hz), 4.66 (1H, dd, J=8, 2.5 Hz), 5.15 (1H, ddd, J=10, 10, 5.5 Hz), 5.96 (1H, s), 7.15 (1H, d, J=10 Hz), 7.16-7.32 (5H, m), 7.44 (1H, d, J=10 Hz);

MASS (ES+): m/e 473.38.

10 Preparation 406

Compound (406) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 220.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.96 (3H, t, J=7.4 Hz), 1.50-1.92 (8H, m), 1.73 (3H, s), 2.17 (1H, m), 2.31 (1H, m), 2.50 (2H, m), 2.95 (1H, dd, J=13.5, 5.5 Hz), 3.19 (1H, m), 3.26 (1H, dd, J=13.5, 10 Hz), 3.88 (1H, m), 4.24 (1H, m), 4.66 (1H, dd, J=7.5, 1.5 Hz), 5.15 (1H, ddd, J=10, 10, 5.5 Hz), 5.90 (1H, s), 7.17 (1H, d, J=10 Hz), 7.17-7.33 (5H, m), 7.39 (1H, d, J=10 Hz), 9.78 (1H, s);

MASS (ES+): m/e 471.39.

20 Preparation 407

Compound (407) was obtained in a manner similar to Preparation 311.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.34-1.98 (18H, m), 2.07-2.39 (4H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.24 (1H, dt, J=10, 7.5 Hz), 4.32 (2H, t, J=6.5 Hz), 4.63-4.74 (2H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.79 (1H, s), 6.77 (2x1H, d, J=8.8 Hz), 7.11 (2x1H, d, J=8.8 Hz), 7.15 (1H, d, J=10 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, d, J=10 Hz), 7.56 (1H, m), 7.06 (2x1H, dd, J=7.5, 1 Hz);

MASS (ES+): m/e 661.37.

Preparation 408

Compound (408) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.24-1.93 (16H, m), 1.28 (3H, s), 2.08-2.39 (4H, m), 2.87 (1H, dd, J=13.5, 6 Hz), 3.17 (1H,

dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.65 (2H, t, J=6.3 Hz), 3.86 (1H, m),  
4.22 (1H, dt, J=10.3, 7.7 Hz), 4.67 (1H, dd, J=8, 2.5 Hz), 4.70 (1H,  
m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.90 (1H, s), 6.77 (2x1H, d, J=9  
5 J=10 Hz);  
MASS (ES+): m/e 557.44.

#### Preparation 409

Compound (409) was obtained in a manner similar to Preparation  
78. The obtained compound was used in Example 223.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.49-  
1.96 (14H, m), 2.07-2.40 (4H, m), 2.50 (2H, m), 2.87 (1H, dd, J=13.5,  
6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.23  
(1H, dt, J=10, 7.5 Hz), 4.63-4.74 (2H, m), 5.13 (1H, ddd, J=10, 10, 6  
Hz), 5.87 (1H, s), 6.77 (2x1H, d, J=8.7 Hz), 7.11 (2x1H, d, J=8.7 Hz),  
15 7.16 (1H, d, J=10 Hz), 7.46 (1H, d, J=10 Hz), 9.77 (1H, s);  
MASS (ES+): m/e 555.45.

#### Preparation 410

Compound (410) was obtained in a manner similar to Preparation  
311.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.36-  
1.99 (8H, m), 2.06-2.39 (4H, m), 2.93 (1H, dd, J=13.5, 6 Hz), 3.21 (1H,  
dd, J=13.5, 10 Hz), 3.28 (1H, m), 3.85 (1H, m), 4.24 (1H, dt, J=10.3,  
7.7 Hz), 4.32 (2H, t, J=6.5 Hz), 4.68 (1H, dd, J=8, 2.5 Hz), 4.74 (2H,  
s), 5.14 (1H, ddd, J=10, 10, 6 Hz), 5.83 (1H, s), 6.90 (2x1H, d, J=8.8  
25 Hz), 7.10 (1H, d, J=10.3 Hz), 7.22 (2x1H, d, J=8.8 Hz), 7.44 (2x1H, dd,  
J=7.5, 7.5 Hz), 7.52-7.60 (2H, m), 8.03 (2x1H, d, J=7.5, 1.5 Hz);  
MASS (ES-): m/e 666.47(M+Cl).

#### Preparation 411

Compound (411) was obtained in a manner similar to Preparation  
30 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.93 (8H, m),  
1.28 (3H, s), 2.08-2.39 (4H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H,  
dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.65 (2H, t, J=6.5 Hz), 3.80 (3H,  
s), 3.85 (1H, m), 4.23 (1H, dt, J=10, 7.5 Hz), 4.60 (2H, s), 4.67 (1H,  
35 m), 5.13 (1H, ddd, J=10, 9.5, 6 Hz), 5.92 (1H, s), 6.82 (2x1H, d,  
J=8.5 Hz), 7.12 (1H, d, J=10 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.53 (1H,

d, J=10 Hz);

MASS (ES+): m/e 561.35.

#### Preparation 412

Compound (412) was obtained in a manner similar to Preparation  
5 78. The obtained compound was used in Example 226.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 1.29 (3H, s), 1.50-  
1.90 (6H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 2.89 (1H, dd, J=13.5,  
5.5 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.80 (3H, s),  
3.85 (1H, m), 4.23 (1H, m), 4.67 (1H, dd, J=8, 2 Hz), 5.13 (1H, ddd,  
10 J=10, 9.5, 5.5 Hz), 5.83 (1H, s), 6.82 (2x1H, d, J=8.5 Hz), 7.13 (1H,  
d, J=10 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.47 (1H, d, J=10 Hz); 9.77 (1H,  
s);

MASS (ES+): m/e 559.29.

#### Preparation 413

15 Compound (413) was obtained in a manner similar to Preparation  
342.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.36-  
1.98 (8H, m), 2.06-2.40 (4H, m), 2.95 (1H, dd, J=13.5, 6 Hz), 3.23 (1H,  
dd, J=13.5, 10 Hz), 3.28 (1H, m), 3.86 (1H, m), 4.24 (1H, dt, J=10, 7.7  
20 Hz), 4.32 (2H, t, J=6 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.18 (1H, m), 5.21  
(1H, dd, J=10.5, 1 Hz), 5.71 (1H, dd, J=17.5, 1 Hz), 5.85 (1H, s), 6.67  
(1H, dd, J=17.5, 10.5 Hz), 7.13 (1H, dd, J=10 Hz), 7.19 (2x1H, d, J=8.2  
Hz), 7.32 (2x1H, d, J=8.2 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52-7.60  
(2H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

25 MASS (ES+): m/e 603.49.

#### Preparation 414

Compound (414) was obtained in a manner similar to Preparation  
77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.24-1.51 (2H, m),  
30 1.28 (3H, s), 1.53-1.94 (6H, m), 2.08-2.40 (4H, m), 2.95 (1H, dd,  
J=13.5, 6 Hz), 3.22 (1H, dd, J=13.5, 10 Hz), 3.27 (1H, m), 3.65 (2H, d,  
J=6 Hz), 3.86 (1H, m), 4.23 (1H, dd, J=10, 7.7 Hz), 4.67 (1H, dd, J=8,  
2 Hz), 5.18 (1H, ddd, J=10, 10, 6 Hz), 5.22 (1H, dd, J=11, 1 Hz), 5.71  
(1H, dd, J=17.5, 1 Hz), 6.00 (1H, s), 6.67 (1H, dd, J=17.5, 11 Hz),  
35 7.13 (1H, d, J=10 Hz), 7.18 (2x1H, d, J=8.2 Hz), 7.32 (2x1H, d, J=8.2  
Hz), 7.56 (1H, d, J=10 Hz);

MASS (ES<sup>+</sup>): m/e 499.58.

Preparation 415

Compound (415) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 231.

- 5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.2 Hz), 1.10 (3x3H, s),  
1.16-1.32 (4H, m), 1.18 (3H, d, J=7 Hz), 1.28 (3H, s), 1.38-1.62 (3H,  
m), 1.70-1.86 (3H, m), 2.08-2.39 (4H, m), 2.51 (2H, m), 2.89 (1H, dd,  
J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.85 (1H,  
m), 4.12-4.24 (2H, m), 4.49 (2H, ddd, J=5, 1.5, 1.5 Hz), 4.67 (1H, m),  
10 5.13 (1H, ddd, J=10.3, 9.5, 6 Hz), 5.27 (1H, ddt, J=10.3, 1.5, 1.5 Hz),  
5.40 (1H, ddt, J=17.2, 1.5, 1.5 Hz), 5.83 (1H, s), 6.04 (1H, ddt,  
J=17.2, 10.3, 5 Hz), 6.82 (2x1H, d, J=8.6 Hz), 7.08 (1H, d, J=10.2 Hz),  
7.14 (2x1H, d, J=8.6 Hz), 7.32-7.48 (6H, m), 7.55 (1H, d, J=10.3 Hz),  
7.58-7.67 (4H, m);  
15 MASS (ES<sup>+</sup>): m/e 837.50.

Preparation 416

Compound (416) was obtained in a manner similar to Preparation 311.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 1.27 (3H, s), 1.36-  
20 1.55 (2H, m), 1.64-1.98 (6H, m), 2.06-2.39 (4H, m), 2.89 (1H, dd,  
J=13.5, 6.5 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (1H,  
m), 4.24 (1H, dt, J=10.3, 7.5 Hz), 4.31 (2H, t, J=6.5 Hz), 4.67 (1H,  
m), 5.13 (1H, m), 5.17 (2H, s), 5.80 (1H, s), 6.90 (2x1H, d, J=8.5 Hz),  
7.13 (1H, d, J=10.3 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.22 (1H, m), 7.44  
25 (2x1H, dd, J=7.5, 7.5 Hz), 7.48-7.60 (3H, m), 7.71 (1H, m), 8.03 (2x1H,  
dd, J=7.5, 1.5 Hz), 8.59 (1H, d, J=4.5 Hz);  
MASS (ES<sup>+</sup>): m/e 684.34.

Preparation 417

- Compound (417) was obtained in a manner similar to Preparation  
30 77.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.30-  
1.94 (9H, m), 2.08-2.40 (4H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H,  
dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.66 (2H, dt, J=6, 5 Hz), 3.85 (1H,  
m), 4.22 (1H, dt, J=10, 7.5 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.13 (1H,  
35 ddd, J=10, 10, 6 Hz), 5.17 (2H, s), 5.86 (1H, s), 6.90 (2x1H, d, J=8.7  
Hz), 7.12 (1H, d, J=10 Hz), 7.14 (2x1H, d, J=8.7 Hz), 7.22 (1H, dd,

J=7.5, 5 Hz), 7.50 (1H, d, J=7.5 Hz), 7.52 (1H, d, J=10 Hz), 7.71 (1H, ddd, J=7.5, 7.5, 2 Hz), 8.58 (1H, dd, J=5, 2 Hz);

MASS (ES+): m/e 579.69.

#### Preparation 418

5 Compound (418) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 234.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 1.29 (3H, s), 1.50-1.92 (6H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.25 (1H, m), 3.85 (1H, m), 4.23  
10 (1H, m), 4.67 (1H, dd, J=8, 2 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.17 (2H, s), 5.88 (1H, s), 6.90 (2x1H, d, J=8.7 Hz), 7.11-7.18 (3H, m), 7.22 (1H, dd, J=7.5, 5 Hz), 7.47 (1H, d, J=10 Hz), 7.50 (1H, d, J=7.5 Hz), 7.71 (1H, ddd, J=7.5, 7.5, 1.8 Hz), 8.59 (1H, dd, J=5, 1.8 Hz), 9.77 (1H, t, J=1 Hz);

15 MASS (ES+): m/e 578.36.

#### Preparation 419

To a 0.5 M solution of isopropenyl magnesium bromide in tetrahydrofuran (61.4 ml) was added a solution of tributyltin chloride (2.5 g) in tetrahydrofuran (8.0 ml) and the mixture was gently  
20 refluxed overnight. The reaction mixture was cooled to ambient temperature. The reaction was quenched by addition of an aqueous saturated ammonium chloride to the mixture. To the reaction mixture was added ice and extracted with hexane. The extract was washed with water and saturated brine and dried over magnesium sulfate. The  
25 magnesium sulfate was filtered off and the extract was evaporated to give the objective Compound (419) as an oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.89 (3x3H, t, J=7 Hz), 1.24-1.60 (18H, m), 5.08 (1H, m), 5.69 (1H, m).

#### Preparation 420

30 Compound (420) was obtained in a manner similar to Preparation 342.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.38-1.53 (2H, m), 1.65-1.99 (6H, m), 2.06-2.40 (4H, m), 2.12 (3H, s), 2.96 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.29 (1H, m),  
35 3.87 (1H, m), 4.24 (1H, dt, J=10.5, 7.5 Hz), 4.32 (2H, t, J=6.5 Hz), 4.68 (1H, dd, J=8, 2 Hz), 5.05 (1H, brs), 5.19 (1H, m), 5.35 (1H, s),

5.90 (1H, s), 7.14 (1H, d, J=10.5 Hz), 7.19 (2x1H, d, J=8.3 Hz), 7.38 (2x1H, d, J=8.3 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52-7.61 (2H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES+): m/e 617.51.

5 Preparation 421

Compound (421) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz; CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.24-1.94 (8H, m), 1.29 (3H, s), 2.08-2.40 (4H, m), 2.12 (3H, s), 2.96 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 10 Hz), 3.29 (1H, m), 3.66 (2H, t, J=6.5 Hz), 3.87 (1H, m), 4.24 (1H, dt, J=10.3, 8 Hz), 4.69 (1H, dd, J=7.5, 1.5 Hz), 5.05 (1H, brs), 5.19 (1H, ddd, J=10, 10, 6 Hz), 5.35 (1H, s), 6.01 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.19 (2x1H, d, J=8 Hz), 7.38 (2x1H, d, J=8 Hz), 7.57 (1H, d, J=10 Hz);

15 MASS (ES+): m/e 513.56.

Preparation 422

Compound (422) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 237.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.50-1.92 (6H, m), 2.08-2.40 (4H, m), 2.12 (3H, s), 2.50 (2H, m), 2.96 (1H, dd, J=13.5, 6.3 Hz), 3.23 (1H, dd, J=13.5, 9.5 Hz), 3.28 (1H, m), 3.87 (1H, m), 4.24 (1H, m), 4.68 (1H, dd, J=7.5, 2 Hz), 5.05 (1H, s), 5.18 (1H, ddd, J=10.3, 9.5, 6.3 Hz), 5.35 (1H, s), 5.95 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.19 (2x1H, d, J=8.3 Hz), 7.38 (2x1H, d, J=8.3 Hz), 7.51 (1H, d, J=10.3 Hz), 9.77 (1H, s);

MASS (ES+): m/e 511.53.

Preparation 423

Compound (423) was obtained in a manner similar to Example 147 mentioned below.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.36-1.55 (2H, m), 1.60-1.98 (6H, m), 2.08-2.40 (4H, m), 2.96 (1H, dd, J=13.5, 6.3 Hz), 3.23 (1H, dd, J=13.5, 9.5 Hz), 3.28 (1H, m), 3.86 (1H, m), 4.25 (1H, dt, J=10.3, 7.7 Hz), 4.32 (1H, t, J=6.7 Hz), 4.62-4.71 (3H, m), 5.18 (1H, m), 5.92 (1H, s), 7.13 (1H, d, J=10.3 Hz), 7.23 (2x1H, d, J=8.5 Hz), 7.28 (2x1H, d, J=8.5 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52-7.62 (2H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES<sup>+</sup>): m/e 607.53.

Preparation 424

To a solution of the Compound (420) in N,N-dimethylformamide (5 ml) were added imidazole (57.9 mg) and then tert-butyldimethylsilyl chloride (103 mg), and the mixture was stirred at ambient temperature for 1 day. To the reaction mixture were added additional imidazole (116 mg), tert-butyldimethylsilyl chloride (210 mg) and 4-(dimethylamino)pyridine (100 mg) and the mixture was stirred at ambient temperature for 4 hours. The mixture was poured into water and extracted with ethyl acetate. The extract was washed with saturated brine (x 2), dried over sodium sulfate, evaporated and purified by preparative thin layer chromatography (eluting with ethyl acetate/hexane = 1/1) to give the objective Compound (424) as a white foam.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.08 (2x3H, s), 0.82 (3H, t, J=7.4 Hz), 0.93 (3x3H, s), 1.28 (3H, s), 1.36-1.56 (2H, m), 1.58-2.00 (6H, m), 2.08-2.40 (4H, m), 2.94 (1H, dd, J=13.5, 6.3 Hz), 3.18-3.31 (2H, m), 3.86 (1H, m), 4.24 (1H, dt, J=10.2, 7.7 Hz), 4.32 (2H, t, J=6.5 Hz), 4.67 (1H, m), 4.69 (2H, s), 5.17 (1H, m), 5.89 (1H, s), 7.13 (1H, d, J=10.2 Hz), 7.19 (2x1H, d, J=8.4 Hz), 7.23 (2x1H, d, J=8.4 Hz), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.52-7.60 (2H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES<sup>+</sup>): m/e 721.50.

Preparation 425

Compound (425) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.08 (2x3H, s), 0.84 (3H, t, J=7.4 Hz), 0.93 (3x3H, s), 1.28 (3H, s), 1.30-1.94 (8H, m), 2.08-2.40 (4H, m), 2.94 (1H, dd, J=13.5, 6 Hz), 3.17-3.31 (2H, m), 3.65 (2H, t, J=6.5 Hz), 3.86 (1H, m), 4.23 (1H, dt, J=10.2, 7.7 Hz), 4.67 (1H, m), 4.69 (2H, s), 5.18 (1H, m), 5.91 (1H, s), 7.13 (1H, d, J=10.2 Hz), 7.19 (2x1H, d, J=8.5 Hz), 7.22 (2x1H, d, J=8.5 Hz), 7.53 (1H, d, J=10.2 Hz);

MASS (ES<sup>+</sup>): m/e 617.61.

Preparation 426

Compound (426) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 240.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.08 (2x3H, s), 0.84 (3H, t, J=7.3 Hz), 0.93 (3x3H, s), 1.29 (3H, s), 1.52-1.92 (6H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 2.94 (1H, dd, J=13.5, 6 Hz), 3.22 (1H, dd, J=13.5, 9.5 Hz), 3.25 (1H, m), 3.86 (1H, m), 4.23 (1H, m), 4.67 (1H, m), 4.69 (2H, s), 5.17 (1H, ddd, J=10.3, 9.5, 6 Hz), 5.90 (1H, s), 7.16 (1H, d, J=10 Hz), 7.18 (2x1H, d, J=8 Hz), 7.23 (2x1H, d, J=8 Hz), 7.49 (1H, d, J=10.3 Hz), 9.77 (1H, t, J=1 Hz);

MASS (ES+): m/e 615.60.

Preparation 427

10 Compound (427) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.12-1.43 (2H, m), 1.36 (9x1/2H, s), 1.39 (9x1/2H, s), 1.48-1.67 (3H, m), 2.06 (1H, m), 2.77 (1/2H, m), 2.93 (1/2H, m), 3.80 (1H, m), 4.53 (1/2H, m), 4.62 (1/2H, m), 12.75 (1H, br);

MASS (ES-): m/e 228.51.

Preparation 428

Compound (428) was obtained in a manner similar to Preparation 119.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.24 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 3.03 (1H, dd, J=14, 6 Hz), 3.07 (1H, dd, J=14, 5 Hz), 3.99 (2H, q, J=7 Hz), 4.16 (2H, q, J=7 Hz), 4.59 (1H, ddd, J=7.5, 6, 5 Hz), 5.09 (1H, d, J=12 Hz), 5.11 (1H, d, J=12 Hz), 5.21 (1H, d, J=7.5 Hz), 6.79 (2x1H, d, J=9 Hz), 7.00 (2x1H, d, J=9 Hz), 7.27-7.40 (5H, m);

25 MASS (ES+): m/e 372.52.

Preparation 429

Compound (429) was obtained in a manner similar to Preparation 77.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.38 (3H, t, J=7 Hz), 3.07 (2H, m), 3.96 (2H, q, J=7 Hz), 4.60 (1H, m), 5.04 (1H, d, J=12 Hz), 5.08 (1H, d, J=12 Hz), 5.23 (1H, br), 6.77 (2x1H, d, J=7.5 Hz), 7.03 (2x1H, d, J=7.5 Hz), 7.20-7.40 (5H, m);

MASS (ES-): m/e 342.57.

Preparation 430

35 Compound (430) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.30-1.64 (8H, m), 1.47 (3x3H, s), 1.65-1.82 (3H, m), 1.95 (1H, m), 2.25 (1H, m), 2.72 (1H, m), 4.25 (2H, t, J=6.3 Hz), 4.67 (1H, m), 4.75 (1H, m), 5.14 (1H, d, J=12.3 Hz), 5.18 (1H, d, J=12.3 Hz), 6.63 (1H, br), 7.30-7.38 (5H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.02 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES<sup>+</sup>): m/e 553.50.

#### Preparation 431

Compound (431) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, DMSO-d<sub>6</sub>, δ): 1.36-1.93 (11H, m), 2.07 (1H, m), 2.89 (1H, m), 3.19 (1H, m), 3.79 (1H, m), 4.25 (2H, t, J=6.3 Hz), 4.38 (1H, m), 5.12 (2H, s), 7.30-7.42 (5H, m), 7.53 (2x1H, dd, J=7.5, 7.5 Hz), 7.67 (1H, m), 7.97 (2x1H, dd, J=7.5, 1.5 Hz), 8.94 (1H, d, J=7.5 Hz);

MASS (ES<sup>+</sup>): m/e 453.52.

#### Preparation 432

Compound (432) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81-0.99 (6H, m), 1.00-2.06 (13H, m), 1.37 (9x2/5H, s), 1.44 (9x3/5H, s), 2.20 (1H, m), 2.46 (1H, m), 3.12 (1H, m), 3.87 (1H, m), 4.15 (1H, m), 4.26 (2H, m), 4.46-4.66 (2.2H, m), 5.04 (0.4H, d, J=7.8 Hz), 5.12 (1H, d, J=12.3 Hz), 5.18 (1H, d, J=12.3 Hz), 5.20-5.29 (1H, m), 6.48 (0.6H, d, J=7.7 Hz), 7.28-7.38 (5H, m), 7.40-7.48 (2H, m), 7.56 (1H, m), 7.98-8.05 (2H, m), 8.28 (0.4H, d, J=7.8 Hz);

MASS (ES<sup>+</sup>): m/e 666.58.

#### Preparation 433

Compound (433) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.90 (3H, m), 1.11 (3H, m), 1.20-2.68 (16H, m), 3.52 (0.5H, m), 3.68 (0.5H, m), 4.24 (2H, m), 4.37-4.62 (2H, m), 5.09 (1H, d, J=12.3 Hz), 5.15 (0.5H, m), 5.18 (1H, d, J=12.3 Hz), 5.36 (0.5H, m), 7.15 (0.5H, m), 7.24-7.37 (5.5H, m), 7.41 (2x1H, dd, J=7.5, 7.5 Hz), 7.54 (1H, m), 8.00 (2x1H, d, J=7.5 Hz), 8.33 (2H, br);

MASS (ES<sup>+</sup>): m/e 566.60.

#### Preparation 434

Compound (434) was obtained in a manner similar to Preparation

16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.66-0.92 (6H, m), 1.10-1.98 (13H, m), 1.39 (3H, t, J=7 Hz), 2.16 (1H, m), 2.47 (1H, m), 2.86-3.04 (2H, m), 3.18 (1H, m), 3.87 (1H, m), 3.91-4.02 (2H, m), 4.22 (2H, t, J=6.5 Hz), 4.30-4.64 (3H, m), 4.82 (0.5H, dd, J=8.5, 6 Hz), 4.99-5.24 (4.5H, m), 5.34 (0.5H, d, J=7 Hz), 5.60 (0.5H, br), 6.40-6.68 (1.5H, m), 6.74-6.82 (2H, m), 7.00-7.12 (2H, m), 7.24-7.48 (12H, m), 7.55 (1H, m), 7.96-8.04 (2H, m), 8.14 (0.5H, d, J=6 Hz);

MASS (ES<sup>+</sup>): m/e 891.42.

10 Preparation 435

Compound (435) was obtained in a manner similar to Preparation 53.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.62-0.84 (6H, m), 1.00-2.03 (14H, m), 1.35 (3H, t, J=7 Hz), 2.50-2.66 (3H, m), 3.07 (1H, m), 3.34 (1H, m), 3.92 (2H, q, J=7 Hz), 4.23 (2H, t, J=6.2 Hz), 4.36-4.86 (4H, m), 6.77 (2x1H, d, J=8.3 Hz), 7.14-7.28 (1H, br), 7.20 (2x1H, d, J=8.3 Hz), 7.40 (2x1H, dd, J=7.5, 7.5 Hz), 7.48-7.70 (2H, m), 7.99 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES<sup>+</sup>): m/e 667.55.

Preparation 436

20 Compound (436) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.68-0.78 (3H, m), 0.78 (3H, d, J=6.5 Hz), 1.04-1.98 (14H, m), 1.38 (3H, t, J=7 Hz), 2.45 (1H, m), 2.69 (1H, m), 2.80 (1H, dd, J=14, 6 Hz), 3.18 (1H, dd, J=14, 10 Hz), 3.95 (2H, q, J=7 Hz), 4.31 (2H, t, J=6.5 Hz), 4.45-4.64 (4H, m), 4.86 (1H, m), 5.85-6.10 (2H, br), 6.22 (1H, d, J=11 Hz), 6.74 (2x1H, d, J=8.5 Hz), 7.08 (2x1H, d, J=8.5 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dddd, J=7.5, 7.5, 1.5, 1.5 Hz), 8.02 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES<sup>+</sup>): m/e 649.51.

30 Preparation 437

Compound (437) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>, δ): 0.67-0.78 (3H, m), 0.79 (3H, d, J=6 Hz), 0.83-1.96 (14H, m), 1.38 (3H, t, J=7 Hz), 2.46 (1H, m), 2.75 (1H, m), 2.80 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.62 (2H, t, J=6.2 Hz), 3.94 (2H, q, J=7 Hz), 4.46-4.65 (4H, m), 4.93 (1H, brd, J=5

Hz), 6.17 (1H, br), 6.44 (1H, br), 6.46 (1H, d, J=10.5 Hz), 6.71 (2x1H, d, J=8.5 Hz), 7.05 (2x1H, d, J=8.5 Hz);

MASS (ES+): m/e 545.50.

Preparation 438

5       Compound (438) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 243.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.67-0.88 (3H, m), 0.79 (3H, d, J=6.7 Hz), 1.09 (1H, m), 1.20-1.47 (3H, m), 1.37 (3H, t, J=7 Hz), 1.54-1.98 (8H, m), 2.46 (1H, m), 2.51 (2H, t, J=7 Hz), 2.74 (1H, m), 2.80 (1H, dd, J=14, 6 Hz), 3.16 (1H, dd, J=14, 10 Hz), 3.92 (2H, q, J=7 Hz), 4.48-4.68 (4H, m), 4.94 (1H, m), 6.21 (1H, br), 6.45 (1H, d, J=10.3 Hz), 6.46 (1H, br), 6.70 (2x1H, d, J=8.8 Hz), 7.05 (2x1H, d, J=8.8 Hz), 9.75 (1H, s);

MASS (ES+): m/e 543.58.

15   Preparation 439

Compound (439) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.30 (3H, d, J=7 Hz), 1.35-1.60 (1H, m), 1.46 (9H, s), 1.71-2.01 (3H, m), 2.62-2.74 (1H, m), 2.94 (1H, dd, J=13, 9 Hz), 3.06 (1H, dd, J=13, 6 Hz), 3.46-3.65 (1H, m), 4.00-4.25 (1H, m), 4.38 (1H, dd, J=8, 4 Hz), 4.95 (1H, ddd, J=9, 8, 1 Hz), 5.09 (1H, d, J=12 Hz), 5.20 (1H, d, J=12 Hz), 5.20 (1H, d, J=7 Hz), 6.81 (1H, d, J=8 Hz), 7.16-7.40 (10H, m);

MASS: m/z 524.38 (M+H)<sup>+</sup>.

25   Preparation 440

Compound (440) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.17-2.03 (10H, m), 1.30 (3H, d, J=7 Hz), 1.43 (9H, s), 2.71-2.86 (1H, m), 3.00 (2H, d, J=7 Hz), 3.51-3.64 (1H, m), 4.01-4.18 (1H, m), 4.31 (2H, t, J=6 Hz), 4.33-4.40 (1H, m), 4.47 (1H, t, J=7 Hz), 4.93 (1H, dt, J=8, 7 Hz), 5.04 (1H, d, J=12 Hz), 5.18 (1H, d, J=12 Hz), 5.18 (1H, d, J=10 Hz), 6.66-6.84 (1H, m), 6.74 (1H, d, J=8 Hz), 7.15-7.38 (10H, m), 7.38-7.48 (2H, m), 7.51-7.60 (1H, m), 8.03 (2H, d, J= 8 Hz);

35   MASS: m/z 757.27 (M+H)<sup>+</sup>.

Preparation 441.

Compound (441) was obtained in a manner similar to Preparation 17.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.12-2.11 (10H, m), 1.25 (3H, d,  $J=7$  Hz), 1.43 (9H, s), 2.88-3.00 (1H, m), 2.99-3.17 (2H, m), 3.82-3.92 (1H, m), 4.01-4.23 (2H, m), 4.35-4.48 (1H, m), 5.01 (1H, dt,  $J=8$ , 7 Hz), 5.25-5.34 (1H, m), 7.15-7.35 (6H, m), 7.43 (2H, t,  $J=8$  Hz), 7.55 (1H, t,  $J=8$  Hz), 8.03 (2H, d,  $J=8$  Hz), 8.25-8.35 (1H, m);

MASS:  $m/z$  667.29 ( $\text{M}+\text{H}$ ) $^+$ .

Preparation 442

Compound (442) was obtained in a manner similar to Preparations 18 and 76.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.27 (3H, d,  $J=7$  Hz), 1.36-1.57 (2H, m), 1.64-1.99 (7H, m), 2.13-2.26 (1H, m), 2.26-2.38 (1H, m), 2.93 (1H, dd  $J=14$ , 10 Hz), 3.16 (1H, dt,  $J=10$ , 7 Hz), 3.22 (1H, dd,  $J=14$ , 10 Hz), 3.90 (1H, dt,  $J=10$ , 4 Hz), 4.31 (2H, t,  $J=7$  Hz), 4.52-4.69 (2H, m), 5.12 (1H, dt,  $J=6$ , 10 Hz), 6.11 (1H, d,  $J=10$  Hz), 6.54 (1H, d  $J=11$  Hz), 7.14-7.34 (5H, m), 7.17 (1H, d,  $J=10$  Hz), 7.44 (1H, dd,  $J=8$ , 7 Hz), 7.56 (1H, t,  $J=7$  Hz), 8.03 (2H, d,  $J=8$  Hz);

MASS:  $m/z$  549.35 ( $\text{M}+\text{H}$ ) $^+$ .

Preparation 443

Compound (443) was obtained in a manner similar to Preparation 77.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.22-1.52 (2H, m), 1.28 (3H, d,  $J=7$  Hz), 1.54-1.96 (7H, m), 2.12-2.27 (1H, m), 2.28-2.39 (1H, m), 2.93 (1H, dd  $J=14$ , 6 Hz), 3.16 (1H, dt,  $J=10$ , 7 Hz), 3.21 (1H, dd,  $J=14$ , 10 Hz), 3.61-3.72 (1H, m), 3.90 (1H, dt,  $J=10$ , 4 Hz), 4.30 (2H, t,  $J=7$  Hz), 4.51-4.62 (2H, m), 4.61-4.69 (1H, m), 5.11 (1H, dt,  $J=6$ , 10 Hz), 6.36 (1H, d,  $J=10$  Hz), 6.60 (1H, d,  $J=10$  Hz), 7.16-7.34 (6H, m);

MASS:  $m/z$  445.36 ( $\text{M}+\text{H}$ ) $^+$ .

Preparation 444

Compound (444) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 246.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.29 (3H, d,  $J=7$  Hz), 1.49-1.96 (6H, m), 2.10-2.41 (2H, m), 2.43-2.57 (2H, m), 2.93 (1H, dd  $J=14$ , 6 Hz), 3.15 (1H, dt,  $J=10$ , 7 Hz), 3.21 (1H, dd,  $J=14$ , 10 Hz), 3.90 (1H, dt,  $J=10$ , 4 Hz), 4.30 (2H, dt,  $J=10$ , 7 Hz), 4.52-4.69 (2H, m), 5.11 (1H, dt,

J=6, 10 Hz), 6.16 (1H, d, J= 10 Hz), 6.53 (1H, d, J= 10 Hz), 7.13-7.33 (6H, m), 9.77 (1H, s);

MASS: m/z 443.37 (M+H)<sup>+</sup>.

Preparation 445

5           Compound (445) was obtained in a manner similar to Preparation 13.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.25 (3H, s), 1.41 (6H, s), 2.90-3.35 (2H, m), 4.59-4.71 (0.5H, m), 4.89-5.01 (0.5H, m), 7.28-7.38 (2H, m), 7.57 (2H, d, J=8.1 Hz);

10       MASS (ES<sup>-</sup>): m/e 332.13 (M-1).

Preparation 446

          Compound (446) was obtained in a manner similar to Preparation 14.

15       <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.30 (2H, s), 1.40 (7H, s), 1.51-1.70 (1H, m), 1.81-2.07 (3H, m), 2.73-3.09 (3H, m), 3.54-3.66 (1H, m), 4.32-4.43 (1H, m), 4.59-4.74 (1H, m), 5.05-5.27 (2H, m), 5.27-5.37 (1H, m), 7.22-7.42 (7H, m), 7.42-7.59 (2H, m);

MASS (ES<sup>+</sup>): m/e 521.33 (M+1).

Preparation 447

20       Compound (447) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.5 Hz), 1.38 (3H, s), 1.43 (9H, s), 1.50-1.68 (1H, m), 1.74-2.03 (5H, m), 2.80-2.95 (1H, m), 3.01-3.14 (2H, m), 3.51-3.68 (1H, m), 4.34-4.41 (1H, m), 4.92-5.02 (1H, m), 5.10 (1H, d, J=12.4 Hz), 5.17 (1H, d, J=12.4 Hz), 6.82-6.91 (0.6H, m), 7.12-7.18 (0.4H, m), 7.12-7.40 (7H, m), 7.40-7.57 (2H, m);

MASS (ES<sup>+</sup>): m/e 620.33 (M+1).

Preparation 448

30       Compound (448) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.73 (3H, t, J=7.3 Hz), 1.39-2.02 (11H, m), 1.43 (3H, s), 1.44 (6H, s), 1.46 (3H, s), 2.07-2.34 (1H, m), 2.86-3.16 (3H, m), 3.49-3.68 (1H, m), 3.90-4.13 (1H, m), 4.30-4.42 (1H, m), 4.31 (2H, t, J=6.2 Hz), 4.93-5.19 (4H, m), 6.79-6.93 (1H, m), 7.29-7.37 (7H, m), 7.39-7.48 (3H, m), 7.49-7.60 (3H, m), 8.00-8.05 (2H, m);

MASS (ES<sup>+</sup>): m/e 853.22 (M+1).

Preparation 449

Compound (449) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.73 (3H, t, J=7.3 Hz), 1.18-2.25 (11H, m),  
5 1.41 (3H, s), 1.44 (9H, s), 2.93-3.20 (2H, m), 3.68-3.82 (1H, m),  
3.94-4.07 (1H, m), 4.07-4.20 (1H, m), 4.27-4.43 (3H, m), 4.94-5.10 (1H,  
m), 5.34 (1H, brs), 6.82 (1H, s), 7.33-7.49 (5H, m), 7.50-7.61 (3H, m),  
8.00-8.09 (2H, m);

MASS (ES<sup>+</sup>): m/e 763.26 (M+1).

10 Preparation 450

Compound (450) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.59-0.73 (3H, m), 1.38 (3H, s), 1.54-2.20  
(12H, m), 2.91-3.22 (3H, m), 3.69-3.82 (1H, m), 4.18-4.41 (4H, m),  
15 4.94-5.08 (1H, m), 7.29-7.58 (7H, m), 7.66-7.82 (1H, m), 7.94-8.05 (2H,  
m), 8.14-8.43 (2H, m);

MASS (ES<sup>+</sup>): m/e 662.30 (Free).

Preparation 451

Compound (451) was obtained in a manner similar to Preparation 20 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.36-  
2.00 (8H, m), 2.02-2.38 (4H, m), 2.98-3.14 (1H, m), 3.22-3.36 (2H, m),  
3.79-3.92 (1H, m), 4.18-4.32 (1H, m), 4.32 (2H, t, J=6.6 Hz), 4.63-  
4.73 (1H, m), 5.13-5.26 (1H, m), 5.82 (1H, s), 7.05 (1H, d, J=10.6 Hz),  
25 7.31-7.40 (2H, m), 7.42 (1H, d, J=8.4 Hz), 7.46 (1H, d, J=8.4 Hz),  
7.50-7.67 (4H, m), 8.03 (2H, d, J=8.4 Hz);

MASS (ES<sup>+</sup>): m/e 645.27 (M+1).

Preparation 452

Compound (452) was obtained in a manner similar to Preparation 30 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.21-1.95 (8H, m),  
1.29 (3H, s), 2.07-2.42 (4H, m), 3.05 (1H, dd, J=13.5, 6.6 Hz), 3.24-  
3.37 (1H, m), 3.28 (1H, dd, J=13.5, 9.2 Hz), 3.66 (2H, t, J=6.3 Hz),  
3.80-3.91 (1H, m), 4.19-4.30 (1H, m), 4.66-4.73 (1H, m), 5.14-5.26 (1H,  
35 m), 5.92 (1H, s), 7.05 (1H, d, J=10.3 Hz), 7.35 (2H, d, J=8.2 Hz),  
7.54 (2H, d, J=8.2 Hz), 7.62 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 541.28 (M+1).

Preparation 453

Compound (453) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 254.

- 5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.49-1.92 (6H, m), 2.09-2.41 (4H, m), 2.51 (2H, t, J=7.3 Hz), 3.04 (1H, dd, J=13.2, 6.6 Hz), 3.25-3.36 (1H, m), 3.28 (1H, dd, J=13.2, 9.9 Hz), 3.81-3.92 (1H, m), 4.18-4.31 (1H, m), 4.65-4.74 (1H, m), 5.14-5.26 (1H, m), 5.85 (1H, s), 7.06 (1H, d, J=10.3 Hz), 7.35 (2H, d, J=8.3 Hz),  
10 7.53-7.63 (1H, m), 7.54 (2H, d, J=8.3 Hz), 9.77 (1H, s);

MASS (ES+): m/e 539.31 (M+1).

Preparation 454

Compound (454) was obtained in a manner similar to Preparation 13.

- 15 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.48 (9H, s), 1.56 (3H, s), 3.21-3.38 (2H, m), 5.05 (1H, brs), 7.10-7.21 (2H, m), 7.22-7.35 (3H, m);

MASS (ES+): m/e 280.14 (M+1).

Preparation 455

- 20 Compound (455) was obtained in a manner similar to Preparation 15.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.36-1.70 (2H, m), 1.41 (2H, s), 1.42 (3H, s), 1.45 (7H, s), 1.73-1.98 (2H, m), 2.57-2.68 (1H, m), 2.82-3.00 (1H, m), 3.01-3.28 (3H, m), 3.48-3.62 (1H, m), 4.32-4.40 (1H, m), 4.74-5.01 (2H, m), 5.10 (1H, d, J=13.6 Hz), 5.16 (1H, d, J=13.6 Hz), 6.67-7.00 (1H, m), 7.05-7.40 (15H, m);

MASS (ES+): m/e 614.39 (M+1).

Preparation 456

Compound (456) was obtained in a manner similar to Preparation 16.

- 30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.11-2.13 (10H, m), 1.44 (9H, s), 1.55 (3H, s), 2.60-2.73 (1H, m), 2.85-3.29 (4H, m), 3.57-3.70 (1H, m), 3.88-4.16 (1H, m), 4.19-4.41 (3H, m), 4.91-5.02 (1H, m), 5.03-5.33 (3H, m), 7.02-7.38 (16H, m), 7.39-7.49 (2H, m), 7.51-7.61 (1H, m), 7.99-8.08 (2H, m);

- 35 MASS (ES+): m/e 847.30 (M+1).

Preparation 457

Compound (457) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.08-2.26 (10H, m), 1.41 (6H, s), 1.42 (6H, s), 2.67-3.15 (1H, m), 2.94-3.15 (3H, m), 3.30-3.44 (1H, m), 3.59-3.74 (1H, m), 3.88-4.02 (1H, m), 4.21-4.40 (3H, m), 4.86-5.00 (1H, m), 5.08-5.25 (1H, m), 6.52 (1H, s), 7.02-7.10 (1H, m), 7.17-7.33 (10H, m), 7.34-7.47 (2H, m), 7.52-7.61 (1H, m), 8.03 (2H, d, J=7.7 Hz);  
MASS (ES+): m/e 757.30 (M+1).

Preparation 458

Compound (458) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.11-2.18 (10H, m), 1.43 (3H, s), 2.68-2.96 (2H, m), 2.98-3.26 (2H, m), 3.62-3.80 (1H, m), 3.96-4.32 (3H, m), 4.32-4.63 (1H, m), 4.64-4.92 (1H, m), 6.94-7.31 (11H, m), 7.31-7.44 (2H, m), 7.44-7.55 (1H, m), 7.80-8.10 (2H, m), 8.18-8.79 (3H, m);  
MASS (ES+): m/e 657.34 (M+1).

Preparation 459

Compound (459) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.30-1.91 (8H, m), 1.72 (3H, s), 1.96-2.17 (1H, m), 2.00-2.34 (1H, m), 2.90-3.00 (2H, m), 3.08-3.30 (3H, m), 3.71-3.83 (1H, m), 4.14-4.43 (1H, m), 4.29 (2H, t, J=6.3 Hz), 4.60-4.66 (1H, m), 5.08-5.20 (1H, m), 6.16 (1H, s), 7.09 (1H, d, J=9.9 Hz), 7.17-7.36 (10H, m), 7.36-7.50 (3H, m), 7.50-7.62 (1H, m), 8.03 (2H, d, J=7.3 Hz);  
MASS (ES+): m/e 639.37 (M+1).

Preparation 460

Compound (460) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.19-1.85 (8H, m), 1.72 (3H, s), 2.00-2.15 (1H, m), 2.21-2.33 (1H, m), 2.93-3.02 (1H, m), 2.95 (1H, d, J=13.9 Hz), 3.12-3.31 (2H, m), 3.18 (1H, d, J=13.9 Hz), 3.62 (2H, t, J=6.3 Hz), 3.72-3.83 (1H, m), 4.11-4.24 (1H, m), 4.59-4.68 (1H, m), 5.08-5.21 (1H, m), 6.15 (1H, s), 7.05 (1H, d, J=10.3 Hz), 7.18-7.40 (10H, m), 7.37 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 535.31 (M+1).

Preparation 461

Compound (461) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 249.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40-1.86 (6H, m), 1.72 (3H, s), 1.98-2.17  
5 (1H, m), 2.20-2.32 (1H, m), 2.36 (1H, t, J=6.6 Hz), 2.46 (1H, t, J=6.6  
Hz), 2.88-3.01 (1H, m), 2.95 (1H, d, J=13.9 Hz), 3.06-3.30 (2H, m),  
3.21 (1H, d, J=13.9 Hz), 3.70-3.84 (1H, m), 4.06-4.32 (1H, m), 4.59-  
4.70 (1H, m), 5.07-5.19 (1H, m), 6.11 (0.2H, s), 6.22 (0.5H, s), 6.39  
10 (0.3H, s), 7.08 (1H, d, J=9.9 Hz), 7.18-7.41 (10H, m), 7.35 (1H, d,  
J=9.5 Hz), 9.73 (1H, s);  
MASS (ES<sup>+</sup>): m/e 533.24 (M+1).

Preparation 462

Compound (462) was obtained in a manner similar to Preparation 13.

15 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.48 (9H, brs), 1.55 (3H, brs), 3.31 (2H,  
brs), 5.04 (1H, brs), 7.10-7.18 (2H, m), 7.21-7.33 (3H, m);  
MASS (ES<sup>+</sup>): m/e 280.12 (M+1).

Preparation 463

Compound (463) was obtained in a manner similar to Preparation 20 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.31 (3H, s), 1.38-1.67 (2H, m), 1.41 (2H,  
s), 1.49 (7H, s), 1.70-1.96 (2H, m), 2.55 (1H, dt, J=9.9, 7.3 Hz),  
2.90 (1H, dd, J=12.8, 10.3 Hz), 3.06-3.23 (1H, m), 3.14 (1H, dd,  
J=12.8, 4.8 Hz), 3.32-3.65 (2H, m), 4.33-4.39 (1H, m), 4.67-4.79 (1H,  
25 m), 4.95 (1H, ddd, J=10.3, 8.4, 4.8 Hz), 5.09 (1H, d, J=12.5 Hz), 5.17  
(1H, d, J=12.5 Hz), 6.95 (1H, d, J=8.4 Hz), 7.06-7.16 (2H, m), 7.18-  
7.41 (13H, m);  
MASS (ES<sup>+</sup>): m/e 614.39 (M+1).

Preparation 464

30 Compound (464) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.30-2.01 (10H, m), 1.41 (9H, s), 1.51 (3H,  
s), 2.62-2.74 (1H, m), 2.87-3.19 (3H, m), 3.36-3.67 (2H, m), 4.00-4.16  
(1H, m), 4.20-4.42 (3H, m), 4.85-5.00 (1H, m), 5.05-5.25 (3H, m),  
35 6.76-7.08 (1H, m), 6.97-7.08 (2H, m), 7.09-7.35 (13H, m), 7.37-7.47  
(2H, m), 7.49-7.59 (1H, m), 7.97-8.06 (2H, m);

MASS (ES+): m/e 847.31 (M+1).

Preparation 465

Compound (465) was obtained in a manner similar to Preparation 17.

- 5  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.09–2.00 (10H, m), 1.41 (9H, s), 1.44 (3H, s), 2.58–2.70 (1H, m), 2.91–3.10 (2H, m), 3.17 (1H, d,  $J=13.9$  Hz), 3.34 (1H, d,  $J=13.9$  Hz), 3.52–3.66 (1H, m), 3.91–4.03 (1H, m), 4.22–4.37 (1H, m), 4.31 (2H, t,  $J=6.3$  Hz), 4.83–4.94 (1H, m), 5.10–5.23 (1H, m), 6.67 (1H, s), 7.03–7.09 (1H, m), 7.16–7.34 (10H, m), 7.38–7.47 (2H, m), 7.52–7.59 (1H, m), 8.03 (2H, d,  $J=7.0$  Hz);

MASS (ES+): m/e 757.33 (M+1).

Preparation 466

Compound (466) was obtained in a manner similar to Preparation 18.

- 15  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.19–2.20 (11H, m), 1.41 (3H, s), 2.79–3.18 (3H, m), 3.30–3.44 (1H, m), 3.58–3.75 (1H, m), 4.02–4.42 (4H, m), 4.83–4.98 (1H, m), 7.05–7.31 (11H, m), 7.32–7.45 (2H, m), 7.45–7.54 (1H, m), 7.97 (2H, d,  $J=7.3$  Hz), 8.04–8.08 (3H, m);

MASS (ES+): m/e 657.38 (Free).

20 Preparation 467

Compound (467) was obtained in a manner similar to Preparation 76.

- $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.17 (3H, s), 1.29–2.39 (10H, m), 3.09 (1H, dd,  $J=13.7$ , 7.0 Hz), 3.23–3.38 (1H, m), 3.31 (1H, dd,  $J=13.7$ , 9.9 Hz), 25 3.39 (1H, d,  $J=13.9$  Hz), 3.61 (1H, d,  $J=13.9$  Hz), 3.81–3.91 (1H, m), 4.18–4.30 (1H, m), 4.34 (2H, t,  $J=6.4$  Hz), 4.67–4.74 (1H, m), 5.22–5.33 (1H, m), 5.93 (1H, s), 6.97–7.05 (2H, m), 7.13–7.35 (9H, m), 7.39–7.48 (2H, m), 7.50–7.59 (1H, m), 7.86 (1H, d,  $J=10.3$  Hz), 8.05 (2H, d,  $J=7.0$  Hz);

- 30 MASS (ES+): m/e 639.35 (M+1).

Preparation 468

Compound (468) was obtained in a manner similar to Preparation 77.

- $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.17 (3H, s), 1.32–1.49 (2H, m), 1.54–2.00 (6H, m), 2.11–2.25 (1H, m), 2.27–2.39 (1H, m), 3.08 (1H, dd,  $J=13.9$ , 7.0 Hz), 3.26–3.38 (1H, m), 3.29 (1H, dd,  $J=13.9$ , 8.8 Hz), 3.38 (1H, d,

J=13.9 Hz), 3.63 (1H, d, J=13.9 Hz), 3.67 (2H, t, J=6.3 Hz), 3.80-3.91 (1H, m), 4.22 (1H, ddd, J=10.3, 8.1, 7.0 Hz), 4.67-4.75 (1H, m), 5.21-5.33 (1H, m), 5.99 (1H, s), 6.99-7.06 (2H, m), 7.15-7.35 (9H, m), 7.86 (1H, d, J=10.3 Hz);

5 MASS (ES+): m/e 535.30 (M+1).

Preparation 469

Compound (469) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 257.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.17 (3H, s), 1.55-1.99 (8H, m), 2.07-2.26  
10 (1H, m), 2.27-2.37 (1H, m), 2.53 (2H, t, J=6.6 Hz), 3.09 (1H, dd, J=13.9, 7.0 Hz), 3.26-3.40 (1H, m), 3.29 (1H, dd, J=13.9, 9.1 Hz), 3.40 (1H, d, J=13.9 Hz), 3.61 (1H, d, J=13.9 Hz), 3.87-3.92 (1H, m), 4.18-4.30 (1H, m), 4.67-4.74 (1H, m), 5.22-5.33 (1H, m), 5.92 (1H, s), 6.98-7.06 (2H, m), 7.15-7.36 (9H, m), 7.81 (1H, d, J=9.9 Hz), 9.79 (1H,  
15 s);

MASS (ES+): m/e 533.24 (M+1).

Preparation 470

Compound (470) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.34 (2H, s), 1.42 (7H, s), 1.60-2.29 (4H, m), 2.85-3.01 (3H, m), 3.57-3.71 (1H, m), 4.36-4.47 (1H, m), 4.57-4.681 (1H, m), 5.11 (1H, d, J=J=12.3 Hz Hz), 5.22 (1H, d, J=J=12.3 Hz), 5.27-5.37 (1H, m), 6.37-7.14 (3H, m), 7.27-7.45 (5H, m);

MASS (ES+): m/e 489.29 (M+1).

25 Preparation 471

Compound (471) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.4 Hz), 1.21-1.49 (14H, m), 1.54-2.09 (5H, m), 2.90-3.04 (2H, m), 3.50-3.71 (2H, m), 4.42 (1H, dd, J=3.3, 8.4 Hz), 4.87-5.06 (1H, m), 5.10 (1H, d, J=12.5 Hz), 5.17 (1H, d, J=12.5 Hz), 6.66-7.13 (4H, m), 7.30-7.42 (5H, m);

MASS (ES+): m/e 588.36 (M+1).

Preparation 472

Compound (472) was obtained in a manner similar to Preparation  
35 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.74 (3H, t, J=7.3 Hz), 1.34-1.46 (9H, m),

1.48-2.33 (16H, m), 2.75-3.09 (2H, m), 3.52-3.75 (2H, m), 3.92-4.13 (1H, m), 4.32 (2H, t, J=6.6 Hz), 4.39-4.45 (1H, m), 4.87-5.10 (1H, m), 5.10-5.21 (2H, m), 6.69-7.11 (4H, m), 7.29-7.37 (6H, m), 7.39-7.49 (2H, m), 7.52-7.63 (1H, m), 8.00-8.06 (2H, m);

5 MASS (ES+): m/e 821.23 (M+1).

Preparation 473

Compound (473) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.3 Hz), 1.42 (3H, s), 1.44 (9H, s), 1.62-1.99 (12H, m), 2.15-2.26 (1H, m), 2.81-3.10 (3H, m), 3.75-3.89 (1H, m), 4.00-4.17 (1H, m), 4.23-4.43 (3H, m), 4.85-4.95 (1H, m), 5.41-5.55 (1H, m), 6.78 (1H, brs), 6.91-7.15 (3H, m), 7.24-7.34 (1H, m), 7.40-7.51 (2H, m), 7.52-7.62 (1H, m), 8.00-8.08 (2H, m);  
MASS (ES+): m/e 731.25 (M+1).

15 Preparation 474

Compound (474) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.63-0.78 (3H, m), 1.37 (3H, s), 1.53-2.16 (15H, m), 2.81-3.28 (3H, m), 3.71-3.86 (1H, m), 4.16-4.42 (4H, m), 4.86-5.01 (1H, m), 6.90-7.14 (3H, m), 7.36-7.46 (2H, m), 7.50-7.59 (1H, m), 7.66-7.83 (1H, m), 8.09-8.33 (3H, m);  
MASS (ES-): m/e 665.32 (M-1).

Preparation 475

Compound (475) was obtained in a manner similar to Preparation 25 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 1.28 (3H, s), 1.36-1.56 (2H, m), 1.63-2.00 (6H, m), 2.06-2.42 (4H, m), 2.93 (1H, dd, J=13.6, 6.6 Hz), 3.18 (1H, dd, J=13.6, 9.3 Hz), 3.30 (1H, dt, J=10.3, 7.3 Hz), 3.80-3.90 (1H, m), 4.20-4.30 (1H, m), 4.32 (2H, t, J=6.3 Hz), 4.66-4.72 (1H, m), 5.12 (1H, dt, J=9.5, 6.6 Hz), 5.86 (1H, s), 6.91-6.99 (1H, m), 7.01-7.12 (3H, m), 7.40-7.48 (2H, m), 7.53-7.63 (2H, m), 8.01-8.06 (2H, m);  
MASS (ES+): m/e 613.28 (M+1).

Preparation 476

35 Compound (476) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.7 Hz), 1.22-1.73 (6H, m), 1.28 (3H, s), 1.74-1.94 (3H, m), 2.08-2.41 (4H, m), 2.92 (1H, dd, J=13.6, 6.6 Hz), 3.18 (1H, dd, J=13.6, 9.2 Hz), 3.30 (1H, dt, J=10.3, 7.3 Hz), 3.66 (2H, t, J=6.2 Hz), 3.85 (1H, ddd, J=10.3, 8.8, 5.1 Hz), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.66-4.72 (1H, m), 5.11 (1H, dt, J=9.2, 6.6 Hz), 5.94 (1H, s), 6.91-6.98 (1H, m), 7.00-7.11 (3H, m), 7.59 (1H, d, J=10.3 Hz);  
MASS (ES<sup>+</sup>): m/e 509.54 (M+1).

Preparation 477

10 Compound (477) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 266.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.45-1.92 (6H, m), 2.07-2.41 (4H, m), 2.46-2.55 (2H, m), 2.92 (1H, dd, J=13.6, 6.6 Hz), 3.18 (1H, dd, J=13.6, 9.2 Hz), 3.30 (1H, dt, J=10.3, 7.0 Hz), 3.79-3.90 (1H, m), 4.24 (1H, dt, J=10.3, 7.0 Hz), 4.65-4.72 (1H, m), 5.12 (1H, ddd, J=10.2, 9.2, 6.6 Hz), 5.86 (1H, s), 6.91-6.98 (1H, m), 7.00-7.12 (3H, m), 7.53 (1H, d, J=10.3 Hz), 9.77 (1H, r, J=1.1 Hz);  
MASS (ES<sup>+</sup>): m/e 507.29 (M+1).

20 Preparation 478

The Compound (343) (1.75 g) was dissolved into tetrahydrofuran (20 ml). To this solution was added (tert-butoxycarbonylmethylene)triphenylphosphoran (2.18 g) and stirred at ambient temperature overnight. The solvent was evaporated and the residue was purified by flash column chromatography (Silica gel 60N, Spherical, 120 g, eluting with ethyl acetate/hexane = 1/1) to give the objective Compound (478) as a white foam.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.38-1.54 (2H, m), 1.53 (3x3H, s), 1.58-1.98 (6H, m), 2.06-2.38 (4H, m), 2.98 (1H, dd, J=13.7, 6.4 Hz), 3.24 (1H, dd, J=13.7, 9.5 Hz), 3.28 (1H, m), 3.85 (1H, m), 4.24 (1H, dt, J=10.3, 7.7 Hz), 4.32 (2H, t, J=6.5 Hz), 4.68 (1H, m), 5.18 (1H, m), 5.89 (1H, s), 6.33 (1H, d, J=16 Hz), 7.10 (1H, d, J=10.3 Hz), 7.24 (2x1H, d, J=8.2 Hz), 7.39-7.48 (4H, m), 7.50-7.62 (3H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);  
MASS (ES<sup>+</sup>): m/e 703.54.

Preparation 479

Compound (479) was obtained in a manner similar to Example 3 mentioned below.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.34-1.54 (2H, m), 1.62-1.97 (6H, m), 2.09-2.38 (4H, m), 2.66 (2H, t, J=7.5 Hz), 2.91 (2H, t, J=7.5 Hz), 2.93 (1H, m), 3.17 (1H, dd, J=13.6, 9.5 Hz), 3.27 (1H, m), 3.84 (1H, m), 4.25 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.70 (1H, m), 5.16 (1H, m), 6.16 (1H, s), 7.11 (2x1H, d, J=8.2 Hz), 7.14 (2x1H, d, J=8.2 Hz), 7.27 (1H, d, J=10.3 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dddd, J=7.5, 7.5, 1.5, 1.5 Hz), 7.65 (1H, d, J=10 Hz), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES+): m/e 705.49.

#### Preparation 480

The Compound (476) (1537 mg) was dissolved in dichloromethane (15 ml). To the mixture was added cold trifluoroacetic acid (5 ml) and stirred at ambient temperature for 30 min. The solvent was evaporated and the residue was azeotropically distilled with toluene. The residue was dissolved in ethyl acetate, washed with saturated brine (x 2) and dried over sodium sulfate. The solvent was removed by evaporation to give the object Compound (480).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.34-1.54 (2H, m), 1.62-1.97 (6H, m), 2.09-2.38 (4H, m), 2.66 (2H, t, J=7.5 Hz), 2.91 (2H, t, J=7.5 Hz), 2.93 (1H, m), 3.17 (1H, dd, J=13.6, 9.5 Hz), 3.27 (1H, m), 3.84 (1H, m), 4.25 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.70 (1H, m), 5.16 (1H, m), 6.16 (1H, s), 7.11 (2x1H, d, J=8.2 Hz), 7.14 (2x1H, d, J=8.2 Hz), 7.27 (1H, d, J=10.3 Hz), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, dddd, J=7.5, 7.5, 1.5, 1.5 Hz), 7.65 (1H, d, J=10 Hz), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES-): m/e 649.56.

#### Preparation 481

Compound (481) was obtained in a manner similar to Preparation 301.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.38-2.00 (14H, m), 2.08-2.40 (4H, m), 2.58 (2H, m), 2.86-2.98 (3H, m), 3.21 (1H, dd, J=14, 9.5 Hz), 3.23-3.38 (3H, m), 3.55 (2H, m), 3.87 (1H, m), 4.24 (1H, m), 4.32 (2H, t, J=6.5 Hz), 4.68 (1H, m), 5.16 (1H, m), 5.87 (1H, s), 7.08-7.19 (5H, m), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.51-

7.60 (2H, m), 8.03 (2x1H, dd, J=7.5, 2 Hz);

MASS (ES+): m/e 716.56.

#### Preparation 482

Compound (482) was obtained in a manner similar to Preparation  
5 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.24-1.93 (14H, m),  
1.28 (3H, s), 2.08-2.40 (4H, m), 2.58 (2H, m), 2.86-2.97 (3H, m), 3.20  
(1H, dd, J=14, 10 Hz), 3.22-3.37 (3H, m), 3.55 (2H, m), 3.65 (2H, t,  
J=6.5 Hz), 3.87 (1H, m), 4.23 (1H, dt, J=10.2, 7.7 Hz), 4.68 (1H, dd,  
10 J=8, 2 Hz), 5.16 (1H, m), 5.94 (1H, s), 7.08-7.18 (5H, m), 7.54 (1H, d,  
J=10.2 Hz);

MASS (ES+): m/e 612.62.

#### Preparation 483

Compound (483) was obtained in a manner similar to Preparation  
15 78. The obtained compound was used in Example 269.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.42-  
1.90 (12H, m), 2.07-2.40 (4H, m), 2.50 (2H, m), 2.58 (2H, m), 2.86-  
2.98 (3H, m), 3.20 (1H, dd, J=14, 9.5 Hz), 3.22-3.38 (3H, m), 3.55 (1H,  
m), 3.87 (1H, m), 4.23 (1H, m), 4.68 (1H, dd, J=8, 2 Hz), 5.16 (1H, m),  
20 5.91 (1H, s), 7.09-7.18 (5H, m), 7.49 (1H, d, J=10 Hz), 9.77 (1H, s);

MASS (ES+): m/e 610.57.

#### Preparation 484

Compound (484) was obtained in a manner similar to Preparation  
303.

25 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.3 Hz), 1.26 (3H, s), 1.36-  
1.98 (8H, m), 2.06-2.38 (4H, m), 2.63 (2H, t, J=7.4 Hz), 2.94 (1H, dd,  
J=13.5, 6.2 Hz), 3.01 (2H, t, J=7.4 Hz), 3.20 (1H, dd, J=13.5, 9.5 Hz),  
3.26 (1H, m), 3.84 (1H, m), 4.24 (1H, m), 4.31 (2H, t, J=6.4 Hz), 4.66  
(1H, m), 5.15 (1H, m), 5.86 (1H, s), 6.98-7.20 (7H, m), 7.30 (2x1H, dd,  
30 J=7.5, 7.5 Hz), 7.39-7.48 (4H, m), 7.51-7.60 (2H, m), 8.03 (2x1H, d,  
J=7.5 Hz);

MASS (ES+): m/e 724.40.

#### Preparation 485

Compound (485) was obtained in a manner similar to Preparation  
35 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.30-

1.93 (8H, m), 2.06-2.38 (4H, m), 2.63 (2H, t, J=7.5 Hz), 2.93 (1H, dd, J=13.7, 6.2 Hz), 3.01 (2H, t, J=7.5 Hz), 3.20 (1H, dd, J=13.7, 9.5 Hz), 3.26 (1H, m), 3.65 (2H, t, J=6.3 Hz), 3.84 (1H, m), 4.22 (1H, dt, J=10, 7.5 Hz), 4.66 (1H, dd, J=8, 2 Hz), 5.15 (1H, ddd, J=10.3, 9.5, 6.2 Hz),  
5 5.93 (1H, s), 7.00-7.20 (7H, m), 7.30 (2x1H, dd, J=7.5, 7.5 Hz), 7.43 (2x1H, d, J=7.5 Hz), 7.54 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 620.50.

#### Preparation 486

Compound (486) was obtained in a manner similar to Preparation  
10 78. The obtained compound was used in Example 272.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.52-1.92 (6H, m), 2.08-2.38 (4H, m), 2.50 (2H, m), 2.63 (2H, t, J=7.5 Hz), 2.93 (1H, dd, J=13.5, 6.2 Hz), 3.01 (2H, t, J=7.5 Hz), 3.20 (1H, dd, J=13.5, 9.5 Hz), 3.25 (1H, m), 3.84 (1H, m), 4.23 (1H, m), 4.66 (1H, dd, J=8, 2 Hz), 5.15 (1H, ddd, J=10.3, 9.5, 6.2 Hz), 5.93 (1H, s),  
15 7.02-7.21 (7H, m), 7.30 (2x1H, dd, J=8, 8 Hz), 7.43 (2x1H, d, J=8 Hz), 7.49 (1H, d, J=10.3 Hz), 9.77 (1H, s);

MASS (ES+): m/e 618.56.

#### Preparation 487

20 Compound (487) was obtained in a manner similar to Preparation 13.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.22 (1H, m), 1.37 (9x1/2H, s), 1.45 (9x1/2H, s), 1.54-1.74 (4H, m), 2.23 (1H, m), 2.80-3.03 (1H, m), 3.82-4.09 (1H, m), 4.75 (1/2H, m), 4.95 (1/2H, m), 5.07-5.25 (2H, m), 7.24-  
25 7.40 (5H, m);

MASS (ES+): m/e 320.48.

#### Preparation 488

Compound (488) was obtained in a manner similar to Preparation 13.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.48-2.34 (6H, m), 3.08 (1H, m), 3.61 (1H, m), 3.99 (1H, dd, J=9, 4 Hz), 5.21 (1H, d, J=12 Hz), 5.26 (1H, d, J=12 Hz), 7.29-7.41 (5H, m);

MASS (ES+): m/e 220.37.

#### Preparation 489

35 Compound (489) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.59 (1H, m), 1.15 (1H, m), 1.30-1.76 (3H, m), 1.42 (3x3H, s), 2.20 (1H, m), 2.90-3.18 (3H, m), 3.57 (1H, m), 4.86-5.00 (1H, m), 5.08-5.24 (3H, m), 5.29 (1H, brd, J=4.5 Hz), 5.44 (1H, d, J=9 Hz), 7.16-7.44 (10H, m);

5 MASS (ES<sup>+</sup>): m/e 467.54.

Preparation 490

Compound (490) was obtained in a manner similar to Preparation 15.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.25 (1H, m), 1.02 (1H, m), 1.18-1.72 (3H, m), 2.14 (1H, m), 3.00-3.24 (2H, m), 3.42 (1H, m), 3.60 (1H, m), 4.88-5.22 (4H, m), 7.17-7.44 (10H, m), 8.60 (2H, br);

MASS (ES<sup>+</sup>): m/e 367.49.

Preparation 491

15 Compound (491) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.58 (1H, m), 1.13 (1H, m), 1.30-1.76 (3H, m), 1.39 (3x3H, s), 2.19 (1H, m), 2.88-3.16 (5H, m), 3.51 (1H, m), 4.35 (1H, m), 4.94 (1H, m), 5.09-5.28 (4H, m), 6.77 (2x1H, d, J=8 Hz), 7.08-7.38 (15H, m);

20 MASS (ES<sup>+</sup>): m/e 614.

Preparation 492

Compound (492) was obtained in a manner similar to Preparation 16.

25 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.43 (1H, m), 1.10 (1H, m), 1.20-1.50 (3H, m), 2.13 (1H, m), 2.89-3.16 (3H, m), 3.20-3.42 (2H, m), 3.52 (1H, m), 4.45 (1H, m), 5.04-5.22 (4H, m), 7.08-7.40 (15H, m), 7.73 (1H, d, J=7.7 Hz), 8.58 (2H, br);

MASS (ES<sup>+</sup>): m/e 514.

Preparation 493

30 Compound (493) was obtained in a manner similar to Preparation 16.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60 (1H, m), 1.14 (1H, m), 1.32-1.90 (9H, m), 1.44 (3x3H, s), 2.20 (1H, m), 2.89-3.06 (4H, m), 3.11 (1H, m), 3.52 (1H, m), 4.07 (1H, m), 4.28 (2H, t, J=6.5 Hz), 4.63 (1H, m), 4.93 (1H, m), 5.06-5.21 (3H, m), 5.26 (1H, brd, J=4.5 Hz), 6.61 (1H, d, J=7.7 Hz), 6.69 (1H, d, J=8 Hz), 7.08-7.38 (15H, m), 7.43 (2x1H, dd,

J=7.5, 7.5 Hz), 7.55 (1H, m), 8.02 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES+): m/e 847.58.

Preparation 494

Compound (494) was obtained in a manner similar to Preparation

5 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.67 (1H, m), 1.12-1.84 (10H, m), 1.42 (3x3H, s), 2.20 (1H, m), 2.87-3.15 (5H, m), 3.56 (1H, m), 4.07 (1H, m), 4.26 (2H, t, J=6.8 Hz), 4.74 (1H, m), 5.00-5.20 (3H, m), 6.85 (2x1H, d, J=8.5 Hz), 7.05-7.32 (10H, m), 7.37-7.48 (3H, m), 7.55 (1H, m), 8.02

10 (2x1H, dd, J=7.5, 1 Hz);

MASS (ES+): m/e 757.

Preparation 495

Compound (495) was obtained in a manner similar to Preparation

18.

15 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.76 (1H, m), 0.98-2.00 (10H, m), 2.14 (1H, m), 2.88-3.10 (5H, m), 3.55 (1H, m), 3.96 (1H, m), 4.14 (2H, m), 4.52 (1H, m), 5.00-5.15 (2H, m), 7.08-7.32 (10H, m), 7.39 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, dd, J=7.5, 7.5 Hz), 7.84 (1H, br), 7.98 (2x1H, d, J=7.5 Hz), 8.24 (2H, br), 8.61 (1H, br);

20 MASS (ES+): m/e 657.

Preparation 496

Compound (496) was obtained in a manner similar to Preparation

76.

25 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.20-2.16 (12H, m), 3.01 (1H, m), 3.08 (1H, dd, J=14, 7 Hz), 3.21 (1H, dd, J=13, 5.5 Hz), 3.26 (1H, dd, J=14, 8 Hz), 3.64 (1H, dd, J=13, 10.5 Hz), 3.72 (1H, ddd, J=10.5, 6, 5.5 Hz), 3.95 (1H, m), 4.20 (1H, m), 4.29 (2H, m), 5.01 (1H, m), 5.36 (1H, m), 6.41 (1H, d, J=6 Hz), 6.48 (1H, d, J=10.5 Hz), 7.05-7.12 (2H, m), 7.14-7.34 (8H, m), 7.39-7.49 (3H, m), 7.56 (1H, m), 8.04 (2H, m);

30 MASS (ES+): m/e 639.33.

Preparation 497

Compound (497) was obtained in a manner similar to Preparation

77.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.88 (10H, m), 1.91-2.15 (2H, m), 2.98 (1H, m), 3.07 (1H, dd, J=14, 7.5 Hz), 3.21 (1H, dd, J=14, 7 Hz), 3.24 (1H, dd, J=14, 8 Hz), 3.55-3.67 (3H, m), 3.76 (1H, m), 3.94 (1H, m),

4.21 (1H, m), 5.04 (1H, m), 5.35 (1H, ddd, J=10, 7.5, 7 Hz), 6.56 (1H, d, J=10.5 Hz), 6.98 (1H, d, J=6 Hz), 7.07-7.14 (8H, m), 7.15-7.34 (8H, m), 7.50 (1H, d, J=10 Hz);

MASS (ES+): m/e 535.36.

5 Preparation 498

Compound (498) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 275.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.24 (1H, m), 1.42-1.88 (7H, m), 1.91-2.15 (2H, m), 2.45 (2H, m), 3.01 (1H, m), 3.07 (1H, dd, J=14, 7.5 Hz), 3.21 (1H, dd, J=13.5, 6 Hz), 3.25 (1H, dd, J=14, 8.5 Hz), 3.63 (1H, dd, J=13.5, 10.5 Hz), 3.76 (1H, ddd, J=10.5, 6, 5.5 Hz), 3.95 (1H, m), 4.20 (1H, m), 5.02 (1H, m), 5.36 (1H, ddd, J=10, 8.5, 7.5 Hz), 6.49 (1H, d, J=10 Hz), 6.53 (1H, d, J=5.5 Hz), 7.06-7.12 (2H, m), 7.16-7.34 (8H, m), 7.39 (1H, d, J=10 Hz), 9.73 (1H, s);

15 MASS (ES-): m/e 531.35.

Preparation 499

Compound (499) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.34 (1H, m), 1.63-1.84 (2H, m), 2.16-2.46 (3H, m), 3.16 (1H, m), 3.66 (1H, m), 4.32 (1H, m), 4.68 (1H, m), 5.05 (1H, d, J=12 Hz), 5.13 (1H, d, J=12 Hz), 7.16-7.38 (10H, m), 8.70 (2H, br);

MASS (ES+): m/e 353.

Preparation 500

25 Compound (500) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40 (3x3H, s), 1.51 (1H, m), 1.72-1.98 (3H, m), 2.62 (1H, m), 2.85-3.13 (4H, m), 3.44 (1H, m), 4.31-4.42 (2H, m), 4.84-4.99 (2H, m), 5.12 (1H, d, J=12.5 Hz), 5.16 (1H, d, J=12.5 Hz), 6.71 (1H, d, J=8 Hz), 7.06-7.40 (15H, m);

30 MASS (ES+): m/e 622.37 (M+Na).

Preparation 501

Compound (501) was obtained in a manner similar to Preparation 16.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.42 (1H, m), 1.65-2.18 (3H, m), 2.54 (1H, m), 2.89-3.60 (5H, m), 4.27 (1H, m), 4.50 (1H, m), 4.79 (1H, m), 5.06-

5.20 (2H, m), 6.85 (1H, m), 7.06-7.40 (14H, m), 8.01 (1H, brd, J=7 Hz),  
8.51 (2H, br);

MASS (ES+): m/e 500.27.

#### Preparation 502

5 Compound (502) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.32-2.25 (10H, m), 1.44 (3x3H, s), 2.62 (1H, m), 2.84-3.11 (4H, m), 3.45 (1H, m), 4.07 (1H, m), 4.29 (2H, t, J=6.5 Hz), 4.36 (1H, m), 4.62 (1H, m), 4.79-5.00 (2H, m), 5.13 (1H, d, J=12 Hz), 5.17 (1H, d, J=12 Hz), 6.56-6.66 (2H, m), 7.10-7.36 (15H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, m), 8.02 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES+): m/e 855.85 (M+Na).

#### Preparation 503

15 Compound (503) was obtained in a manner similar to Preparation 17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.33-2.12 (10H, m), 1.42 (3x3H, s), 2.76 (1H, m), 2.87 (1H, dd, J=14, 5 Hz), 3.02-3.22 (3H, m), 3.60 (1H, m), 4.11 (1H, m), 4.22 (1H, m), 4.28 (2H, t, J=6.5 Hz), 4.85 (1H, m), 4.94 (1H, d, J=8.5 Hz), 5.12 (1H, m), 6.91 (1H, d, J=7.7 Hz), 6.99 (2x1H, d, J=7 Hz), 7.08-7.32 (8H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, m), 8.03 (2x1H, d, J=7.5 Hz), 8.31 (1H, brd, J=8.5 Hz);

MASS (ES-): m/e 741.96.

#### Preparation 504

25 Compound (504) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.02-2.05 (10H, m), 2.72-3.18 (5H, m), 3.53 (1H, m), 3.93-4.30 (4H, m), 4.62 (1H, m), 4.84 (1H, m), 7.04-7.32 (11H, m), 7.39 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, dd, J=7.5, 7.5 Hz), 7.98 (2x1H, d, J=7.5 Hz), 8.30 (2H, br), 8.54 (1H, br);

MASS (ES+): m/e 643.78.

#### Preparation 505

Compound (505) was obtained in a manner similar to Preparation 76.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.31-1.45 (2H, m), 1.60-1.98 (6H, m), 2.08-2.36 (2H, m), 3.02 (1H, dd, J=14, 6 Hz), 3.16-3.36 (3H, m), 3.60-3.79

(2H, m), 3.86 (1H, m), 4.18 (1H, m), 4.29 (1H, t, J=6 Hz), 4.67 (1H, m), 5.16 (1H, m), 6.38 (1H, d, J=5 Hz), 7.08-7.34 (11H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.48-7.60 (2H, m), 8.03 (2x1H, d, J=7.5 Hz);  
MASS (ES+): m/e 625.54.

5 Preparation 506

Compound (506) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.22-1.39 (2H, m), 1.46-1.94 (6H, m), 2.07-2.37 (2H, m), 3.02 (1H, dd, J=13.5, 6 Hz), 3.22 (1H, m), 3.27 (1H, dd, J=13.5, 9 Hz), 3.31 (1H, dd, J=13.5, 6 Hz), 3.63 (2H, t, J=6.5 Hz), 3.68 (1H, dd, J=13.5, 10.5 Hz), 3.74 (1H, ddd, J=10.5, 6, 6 Hz), 3.85 (1H, m), 4.18 (1H, m), 4.68 (1H, m), 5.16 (1H, ddd, J=10, 9, 6 Hz), 6.52 (1H, d, J=6 Hz), 7.10-7.34 (11H, m), 7.53 (1H, d, J=10 Hz);  
MASS (ES+): m/e 519.90.

15 Preparation 507

Compound (507) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 281.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.42-1.96 (6H, m), 2.06-2.37 (2H, m), 2.45 (2H, m), 3.02 (1H, dd, J=14, 6 Hz), 3.22 (1H, m), 3.27 (1H, dd, J=14, 10 Hz), 3.32 (1H, dd, J=13, 6 Hz), 3.67 (1H, dd, J=13, 10 Hz), 3.75 (1H, ddd, J=10, 6, 5 Hz), 3.86 (1H, m), 4.18 (1H, m), 4.68 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 6.45 (1H, d, J=5 Hz), 7.10-7.40 (11H, m), 7.49 (1H, d, J=10 Hz), 9.74 (1H, s);  
MASS (ES+): m/e 519.94.

25 Preparation 508

Compound (508) was obtained in a manner similar to Preparation 13.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.24 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 1.42 (3x3H, s), 3.02 (2H, m), 4.00 (2H, q, J=7 Hz), 4.16 (2H, q, J=7 Hz), 4.51 (1H, m), 4.96 (1H, brd, J=7 Hz), 6.81 (2x1H, d, J=8.7 Hz), 7.03 (2x1H, d, J=8.7 Hz);  
MASS (ES+): m/e 338.47.

Preparation 509

Compound (509) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40 (3H, t, J=7 Hz), 1.42 (3x3H, s), 3.03

(1H, dd, J=14, 6 Hz), 3.12 (1H, dd, J=14, 5.5 Hz), 4.01 (2H, q, J=7 Hz), 4.55 (1H, m), 4.92 (1H, brd, J=7.5 Hz), 6.83 (2x1H, d, J=8.5 Hz), 7.08 (2x1H, d, J=8.5 Hz);  
MASS (ES-): m/e 308.50.

5 Preparation 510

Compound (510) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.58 (1H, m), 1.04-1.76 (4H, m), 1.38 (3H, t, J=7 Hz), 1.40 (3x3H, s), 2.19 (1H, m), 2.84-3.14 (5H, m), 3.51 (1H, m), 3.98 (2H, q, J=7 Hz), 4.31 (1H, m), 4.92 (1H, m), 5.08-5.23 (3H, m), 5.25 (1H, d, J=4 Hz), 6.75-6.85 (3H, m), 6.96-7.11 (3H, m), 7.13-7.41 (9H, m);  
MASS (ES+): m/e 658.

Preparation 511

15 Compound (511) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.44 (1H, m), 1.00-2.19 (5H, m), 1.30 (3H, t, J=7 Hz), 2.88-3.58 (6H, m), 3.86 (2H, q, J=7 Hz), 4.41 (1H, m), 4.86-5.22 (4H, m), 6.65 (1/3H, d, J=8.5 Hz), 6.74 (5/3H, d, J=8.5 Hz), 20 6.89 (1/3H, d, J=8.5 Hz), 7.10-7.36 (35/3H, m), 7.82 (5/6H, d, J=7.5 Hz), 8.26 (1/6H, d, J=7.5 Hz), 8.52 (2H, br);  
MASS (ES+): m/e 558.

Preparation 512

25 Compound (512) was obtained in a manner similar to Preparation 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.60 (1H, m), 1.14 (1H, m), 1.30-1.90 (9H, m), 1.37 (3H, t, J=7 Hz), 1.43 (3x3H, s), 2.20 (1H, m), 2.87-3.04 (4H, m), 3.10 (1H, m), 3.52 (1H, m), 3.96 (2H, q, J=7 Hz), 4.07 (1H, m), 4.29 (2H, t, J=6.5 Hz), 4.59 (1H, m), 4.94 (1H, m), 5.07-5.22 (3H, m), 30 5.26 (1H, brd, J=5 Hz), 6.58 (1H, d, J=8 Hz), 6.70 (1H, d, J=7.5 Hz), 6.79 (2x1H, d, J=8.5 Hz), 7.04 (2x1H, d, J=8.5 Hz), 7.09-7.38 (10H, m), 7.42 (2x1H, dd, J=7.5, 7.5 Hz), 7.54 (1H, m), 8.02 (2x1H, dd, J=7.5, 1 Hz);  
MASS (ES+): m/e 891.

35 Preparation 513

Compound (513) was obtained in a manner similar to Preparation

17.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.67 (1H, m), 1.10-1.88 (10H, m), 1.36 (3H, t,  $J=7$  Hz), 1.42 (3x3H, s), 2.20 (1H, m), 2.88-3.13 (5H, m), 3.52 (1H, m), 3.93 (2H, q,  $J=7$  Hz), 4.06 (1H, m), 4.27 (2H, t,  $J=6.5$  Hz), 4.68 (1H, m), 4.98-5.18 (3H, m), 6.69-6.81 (3H, m), 7.00 (2x1H, d,  $J=8.5$  Hz), 7.10-7.34 (6H, m), 7.43 (2x1H, dd,  $J=7.5$ , 7.5 Hz), 7.55 (1H, m), 8.02 (2x1H, dd,  $J=7.5$ , 1.5 Hz);

MASS (ES+): m/e 800.

Preparation 514

10 Compound (514) was obtained in a manner similar to Preparation 18.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.76 (1H, m), 1.02-2.02 (10H, m), 1.27 (3H, t,  $J=7$  Hz), 2.13 (1H, m), 2.85-3.12 (5H, m), 3.54 (1H, m), 3.83 (2H, br-q,  $J=7$  Hz), 3.98 (1H, br), 4.15 (2H, br), 4.46 (1H, br), 4.99-5.15 (2H, m), 6.70 (2x1H, d,  $J=8$  Hz), 7.06 (2x1H, d,  $J=8$  Hz), 7.14-7.32 (5H, m), 7.38 (2x1H, dd,  $J=7.5$ , 7.5 Hz), 7.51 (1H, dd,  $J=7.5$ , 7.5 Hz), 7.81 (1H, br), 7.98 (2x1H, d,  $J=7.5$  Hz), 8.26 (2H, br), 8.56 (1H, br);

MASS (ES+): m/e 701.

Preparation 515

20 Compound (515) was obtained in a manner similar to Preparation 76.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.14-2.16 (12H, m), 1.37 (3H, t,  $J=7$  Hz), 3.01 (1H, m), 3.08 (1H, dd,  $J=14$ , 7 Hz), 3.15 (1H, dd,  $J=13.5$ , 6 Hz), 3.25 (1H, dd,  $J=14$ , 8 Hz), 3.55 (1H, dd,  $J=13.5$ , 10.5 Hz), 3.67 (1H, ddd,  $J=8$ , 6, 6 Hz), 3.94 (1H, m), 3.94 (2H, q,  $J=7$  Hz), 4.21 (1H, m), 4.30 (2H, m), 5.02 (1H, m), 5.36 (1H, m), 6.44 (1H, d,  $J=6$  Hz), 6.48 (1H, d,  $J=10$  Hz), 6.73 (2x1H, d,  $J=8.5$  Hz), 6.98 (2x1H, d,  $J=8.5$  Hz), 7.18-7.34 (5H, m), 7.37-7.48 (3H, m), 7.55 (1H, m), 8.03 (2x1H, dd,  $J=8$ , 1.5 Hz);

30 MASS (ES+): m/e 683.43.

Preparation 516

Compound (516) was obtained in a manner similar to Preparation 77.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.14-1.85 (10H, m), 1.39 (3H, t,  $J=7$  Hz), 1.96 (1H, m), 2.07 (1H, m), 2.90-3.29 (4H, m), 3.47-3.75 (4H, m), 3.94 (1H, m), 3.98 (1H, q,  $J=7$  Hz), 4.20 (1H, m), 5.03 (1H, m), 5.35 (1H,

m), 6.53 (1H, d, J=10 Hz), 6.76 (2x1H, d, J=8.5 Hz), 6.79 (2x1H, d, J=6.5 Hz), 6.99 (2x1H, d, J=8.5 Hz), 7.18-7.34 (5H, m), 7.45 (1H, d, J=10.5 Hz);

MASS (ES+): m/e 579.38.

5 Preparation 517

Compound (517) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 287.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.86 (8H, m), 1.39 (3H, t, J=7 Hz), 1.91-2.16 (2H, m), 2.46 (2H, m), 2.93-3.30 (4H, m), 3.54 (1H, d, J=14, 11 Hz), 3.71 (1H, m), 3.94 (1H, m), 3.98 (1H, q, J=7 Hz), 4.20 (1H, m), 5.02 (1H, m), 5.35 (1H, m), 6.49 (1H, d, J=10 Hz), 6.50 (1H, d, J=5.5 Hz), 6.76 (2x1H, d, J=8.5 Hz), 6.99 (2x1H, d, J=8.5 Hz), 7.15-7.35 (5H, m), 7.36 (1H, d, J=10 Hz), 9.74 (1H, s);

MASS (ES+): m/e 577.33.

15 Preparation 518

Compound (518) was obtained in a manner similar to Preparation 14.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (1H, m), 1.17 (1H, m), 1.30-1.74 (3H, m), 1.39 (3H, t, J=7 Hz), 1.42 (3x3H, s), 2.21 (1H, m), 2.83-2.97 (2H, m), 3.13 (1H, m), 3.59 (1H, m), 3.99 (2H, q, J=7 Hz), 4.87 (1H, m), 5.08-5.23 (2H, m), 5.29 (1H, m), 5.42 (1H, d, J=8.5 Hz), 6.74 (0.2H, d, J=8.5 Hz), 6.80 (1.8H, d, J=8.5 Hz), 6.96 (0.2H, d, J=8.5 Hz), 7.09 (1.8H, d, J=8.5 Hz), 7.24-7.41 (5H, m);

MASS (ES+): m/e 511.29.

25 Preparation 519

Compound (519) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.49 (1H, m), 1.07 (1H, m), 1.22-1.74 (3H, m), 1.34 (3x1/7H, t), 1.36 (3x6/7H, t, J=7 Hz), 2.13 (1H, m), 3.00-3.31 (2H, m), 3.41-3.54 (2H, m), 3.89 (2x1/7H, q, J=7 Hz), 3.95 (2x6/7H, q, J=7 Hz), 4.84-5.22 (4H, m), 6.73 (2x1/7H, d, J=8.5 Hz), 6.79 (2x6/7H, d, J=8.5 Hz), 7.21 (2x1H, d, J=8.5 Hz), 7.25-7.40 (5H, m), 8.29 (2x1/7H, br), 8.57 (2x6/7H, br);

MASS (ES+): m/e 411.20.

35 Preparation 520

Compound (520) was obtained in a manner similar to Preparation

15.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.71 (1H, m), 1.06–1.70 (19H, m), 2.21 (1H, m), 2.82–3.16 (5H, m), 3.54 (1H, m), 3.91–4.04 (4H, m), 4.30 (1H, m), 4.92 (1H, m), 5.08–5.18 (3H, m), 5.26 (1H, m), 6.68–6.90 (5H, m),

5 7.00–7.12 (4H, m), 7.24–7.40 (5H, m);

MASS (ES+): m/e 702.35.

Preparation 521

Compound (521) was obtained in a manner similar to Preparation 16.

10  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.58 (1H, m), 1.02–1.60 (10H, m), 2.15 (1H, m), 2.83–3.32 (5H, m), 3.56 (1H, m), 3.80–4.02 (4H, m), 4.38 (1H, m), 5.02–5.22 (4H, m), 6.63–6.93 (4H, m), 7.07 (2x1H, d,  $J=8.5$  Hz), 7.16 (2x1H, d,  $J=8.5$  Hz), 7.24–7.40 (5H, m), 7.71 (1x5/6H, brd,  $J=7$  Hz), 8.19 (1x1/6H, brd,  $J=7$  Hz), 8.50 (2H, br);

15 MASS (ES+): m/e 602.28.

Preparation 522

Compound (522) was obtained in a manner similar to Preparation 16.

20  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.71 (1H, m), 1.06–1.90 (10H, m), 1.37 (3H, t,  $J=7$  Hz), 1.38 (3H, t,  $J=7$  Hz), 1.43 (3x3H, s), 2.21 (1H, m), 2.82–3.03 (4H, m), 3.12 (1H, m), 3.54 (1H, m), 3.95 (2H, q,  $J=7$  Hz), 3.97 (2H, q,  $J=7$  Hz), 4.07 (1H, m), 4.28 (2H, t,  $J=6.5$  Hz), 4.59 (1H, m), 4.92 (1H, m), 5.05–5.21 (3H, m), 5.27 (1H, brd,  $J=4$  Hz), 6.56 (1H, d,  $J=6.5$  Hz), 6.61–6.88 (5H, m), 6.96–7.09 (4H, m), 7.24–7.38 (5H, m),  
25 7.42 (2x1H, dd,  $J=7.5$ , 7.5 Hz), 7.54 (1H, dd,  $J=7.5$ , 7.5 Hz), 8.02 (2x1H, d,  $J=7.5$  Hz);

MASS (ES-): m/e 968.89 (M+Cl).

Preparation 523

Compound (523) was obtained in a manner similar to Preparation 17.

30  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.78 (1H, m), 1.18–1.88 (10H, m), 1.35 (3H, t,  $J=7$  Hz), 1.38 (3H, t,  $J=7$  Hz), 1.41 (3x3H, s), 2.21 (1H, m), 2.82–3.01 (4H, m), 3.09 (1H, m), 3.54 (1H, m), 3.93 (2H, q,  $J=7$  Hz), 3.98 (2H, q,  $J=7$  Hz), 4.16 (1H, m), 4.27 (2H, t,  $J=6.5$  Hz), 4.68 (1H, m),  
35 5.00–5.20 (3H, m), 6.67–6.83 (5H, m), 7.00 (2x1H, d,  $J=8.5$  Hz), 7.06 (2x1H, d,  $J=8.5$  Hz), 7.29 (1H, d,  $J=7.5$  Hz), 7.43 (2x1H, dd,  $J=7.5$ ,

7.5 Hz), 7.55 (1H, dd, J=7.5, 7.5 Hz), 8.02 (2x1H, d, J=7.5 Hz);

MASS (ES+): m/e 845.27.

#### Preparation 524

Compound (524) was obtained in a manner similar to Preparation

5 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.75-2.01 (11H, m), 1.28 (3H, t, J=7 Hz),  
1.35 (3H, t, J=7 Hz), 2.14 (1H, m), 2.80-3.12 (5H, m), 3.55 (1H, m),  
3.74-4.02 (5H, m), 4.15 (2H, br), 4.46 (1H, m), 4.97-5.12 (2H, m),  
6.71 (2x1H, brd, J=8 Hz), 6.77 (2x1H, brd, J=8 Hz), 7.00-7.20 (4H, m),  
10 7.38 (2x1H, dd, J=7.5, 7.5 Hz), 7.51 (1H, dd, J=7.5, 7.5 Hz), 7.98  
(2x1H, d, J=7.5 Hz), 8.26 (2H, br);

MASS (ES+): m/e 745.28.

#### Preparation 525

Compound (525) was obtained in a manner similar to Preparation

15 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-2.17 (12H, m), 1.37 (3H, t, J=7 Hz),  
1.40 (3H, t, J=7 Hz), 2.92-3.06 (2H, m), 3.11-3.24 (2H, m), 3.54 (1H,  
dd, J=13.5, 10.5 Hz), 3.68 (1H, m), 3.87-4.05 (1H, m), 3.94 (2H, q,  
J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.21 (1H, m), 4.29 (2H, t, J=6.5 Hz),  
20 5.02 (1H, m), 5.30 (1H, m), 6.50 (1H, d, J=10 Hz), 6.53 (1H, d, J=5.5  
Hz), 6.73 (2x1H, d, J=8.8 Hz), 6.82 (2x1H, d, J=8.8 Hz), 6.98 (2x1H, d,  
J=8.8 Hz), 7.16 (2x1H, d, J=8.8 Hz), 7.41 (1H, d, J=10.5 Hz), 7.44  
(2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=7.5, 1 Hz);  
MASS (ES+): m/e 727.19.

25 Preparation 526

Compound (526) was obtained in a manner similar to Preparation

77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.87 (10H, m), 1.39 (3H, t, J=7 Hz),  
1.40 (3H, t, J=7 Hz), 1.90-2.16 (2H, m), 2.92-3.05 (2H, m), 3.16 (1H,  
30 dd, J=14, 6 Hz), 3.18 (1H, dd, J=14, 8 Hz), 3.55 (1H, dd, J=14, 10.5  
Hz), 3.62 (1H, t, J=6 Hz), 3.70 (1H, ddd, J=10.5, 6, 6 Hz), 3.95 (1H,  
m), 3.98 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.19 (1H, m), 5.02 (1H,  
m), 5.29 (1H, m), 6.51 (1H, d, J=10.5 Hz), 6.67 (1H, d, J=6 Hz), 6.75  
(2x1H, d, J=9 Hz), 6.82 (2x1H, d, J=8.5 Hz), 6.99 (2x1H, d, J=9 Hz),  
35 7.15 (2x1H, d, J=8.5 Hz), 7.42 (1H, d, J=10 Hz);  
MASS (ES+): m/e 623.98.

Preparation 527

Compound (527) was obtained in a manner similar to Preparation 78. The obtained compound was used in Examples 293 and 296.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.87 (8H, m), 1.39 (3H, t, J=7 Hz),  
5 1.40 (3H, t, J=7 Hz), 1.90-2.16 (2H, m), 2.46 (2H, t, J=6.5 Hz), 2.91-  
3.06 (2H, m), 3.10-3.24 (2H, m), 3.53 (1H, dd, J=14, 10.5 Hz), 3.72  
(1H, m), 3.94 (1H, m), 3.99 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz),  
4.21 (1H, m), 5.02 (1H, m), 5.30 (1H, m), 6.50 (1H, d, J=10 Hz), 6.61  
(1H, d, J=6 Hz), 6.76 (2x1H, d, J=8.5 Hz), 6.82 (2x1H, d, J=8.5 Hz),  
10 6.99 (2x1H, d, J=8.5 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.34 (1H, d, J=10  
Hz), 9.74 (1H, s);

MASS (ES<sup>+</sup>): m/e 621.45.

Preparation 528

Compound (528) was obtained in a manner similar to Preparation  
15 119.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.24 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz),  
3.02 (2H, m), 4.01 (2H, q, J=7 Hz), 4.16 (2H, q, J=7 Hz), 4.51 (1H, m),  
4.96 (1H, brd, J=8 Hz), 6.81 (2x1H, d, J=8.4 Hz), 7.03 (2x1H, d, J=8.4  
Hz);

20 MASS (ES<sup>+</sup>): m/e 338.51.

Preparation 529

Compound (529) was obtained in a manner similar to Preparation  
17.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40 (3H, t, J=7 Hz), 1.42 (3x3H, s), 3.08  
25 (2H, m), 4.01 (2H, q, J=7 Hz), 4.54 (1H, m), 4.91 (8H, brd), 6.83  
(2x1H, d, J=8.8 Hz), 7.09 (2x1H, d, J=8.8 Hz);

MASS (ES<sup>-</sup>): m/e 338.55.

Preparation 530

Compound (530) was obtained in a manner similar to Preparation  
30 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.32-1.96 (4H, m), 1.38 (3H, t, J=7 Hz),  
1.40 (3x3H, s), 2.56 (1H, m), 2.77 (1H, dd, J=13, 10 Hz), 2.82-3.09  
(3H, m), 3.49 (1H, m), 3.98 (2H, q, J=7 Hz), 4.27-4.40 (2H, m), 4.83-  
5.03 (2H, m), 5.10 (1H, d, J=12 Hz), 5.18 (1H, d, J=12 Hz), 6.66 (1H,  
35 brd, J=8 Hz), 6.82 (2x1H, d, J=8.7 Hz), 7.08 (2x1H, d, J=8.7 Hz),  
7.14-7.41 (10H, m);

MASS (ES+): m/e 644.50.

Preparation 531

Compound (531) was obtained in a manner similar to Preparation 16.

5  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.22-2.28 (7H, m), 2.76 (1H, m), 2.85-3.34 (4H, m), 3.60 (1H, m), 3.74-4.04 (2H, m), 4.42 (1H, m), 4.68 (1H, m), 4.90-5.08 (2H, m), 5.17 (1H, d,  $J=12$  Hz), 6.44-6.60 (2H, m), 6.73 (2x1H, d,  $J=8.5$  Hz), 7.14-7.48 (10H, m), 7.86 (2H, br), 9.04 (1H, br);  
MASS (ES+): m/e 544.50.

10 Preparation 532

Compound (532) was obtained in a manner similar to Preparation 16.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.29-1.95 (10H, m), 1.35 (3H, t,  $J=7$  Hz), 1.43 (3x3H, s), 2.62 (1H, m), 2.72-3.06 (4H, m), 3.53 (1H, m), 3.95 (2H, q,  $J=7$  Hz), 4.06 (1H, m), 4.27 (2H, t,  $J=6.5$  Hz), 4.31 (1H, m), 4.66 (1H, m), 4.89 (1H, m), 5.10 (1H, d,  $J=12$  Hz), 5.14 (1H, m), 5.16 (1H, d,  $J=12$  Hz), 6.64-6.84 (2H, m), 6.80 (2x1H, d,  $J=8.8$  Hz), 7.06 (2x1H, d,  $J=8.8$  Hz), 7.12-7.47 (12H, m), 7.54 (1H, m), 8.03 (2x1H, dd,  $J=8, 1.5$  Hz);  
20 MASS (ES+): m/e 877.31.

Preparation 533

Compound (533) was obtained in a manner similar to Preparation 17.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.28-1.90 (9H, m), 1.36 (3H, t,  $J=7$  Hz), 25 1.41 (3x3H, s), 2.09 (1H, m), 2.66 (1H, m), 2.84-3.05 (4H, m), 3.69 (1H, m), 3.96 (2H, q,  $J=7$  Hz), 4.05 (1H, m), 4.21-4.36 (3H, m), 4.69 (1H, m), 4.80 (1H, m), 5.27 (1H, m), 6.78 (2x1H, d,  $J=8.7$  Hz), 6.87 (1H, m), 7.04 (2x1H, brd,  $J=8.7$  Hz), 7.13-7.33 (5H, m), 7.39-7.49 (3H, m), 7.55 (1H, m), 8.02 (2x1H, dd,  $J=8, 1.5$  Hz);  
30 MASS (ES+): m/e 787.42.

Preparation 534

Compound (534) was obtained in a manner similar to Preparation 18.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 1.16-1.96 (10H, m), 1.27 (3H, t,  $J=7$  Hz), 35 2.70-3.14 (5H, m), 3.66 (1H, m), 3.84 (2H, q,  $J=7$  Hz), 4.05-4.36 (4H, m), 4.59 (1H, m), 5.06 (1H, m), 6.73 (2x1H, d,  $J=8.5$  Hz), 7.08-7.28

(8H, m), 7.40 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, dd, J=7.5, 7.5 Hz), 7.95-8.32 (3H, m), 8.02 (2x1H, d, J=7.5 Hz);

MASS (ES+): m/e 687.52.

Preparation 535

5 Compound (535) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.34-1.52 (2H, m), 1.39 (3H, t, J=7 Hz), 1.56-1.95 (6H, m), 2.11-2.39 (2H, m), 2.77 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13, 5 Hz), 3.02-3.24 (3H, m), 3.94 (1H, m), 3.98 (2H, q, J=7 Hz), 4.24-4.35 (2H, m), 4.61 (1H, dd, J=8, 2.5 Hz), 4.69 (1H, m), 5.06 (1H, m), 6.31 (1H, d, J=10 Hz), 6.46 (1H, d, J=10.5 Hz), 6.80 (2x1H, d, J=8.8 Hz), 7.11 (2x1H, d, J=8.8 Hz), 7.14-7.30 (6H, m), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

15 MASS (ES+): m/e 669.43.

Preparation 536

Compound (536) was obtained in a manner similar to Preparation 77:

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.25-1.92 (8H, m), 1.40 (3H, t, J=7 Hz), 2.13-2.40 (2H, m), 2.77 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13.5, 5 Hz), 3.02-3.24 (3H, m), 3.63 (2H, t, J=6.5 Hz), 3.94 (1H, m), 4.00 (2H, q, J=7 Hz), 4.28 (1H, m), 4.62 (1H, m), 4.69 (1H, m), 5.06 (1H, ddd, J=10, 10, 5 Hz), 6.40 (1H, d, J=10 Hz), 6.49 (1H, d, J=10 Hz), 6.81 (2x1H, d, J=8.7 Hz), 7.11 (2x1H, d, J=8.7 Hz), 7.15-7.32 (6H, m);

25 MASS (ES+): m/e 565.49.

Preparation 537

Compound (537) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 299..

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.40 (3H, t, J=7 Hz), 1.48-1.90 (6H, m), 2.12-2.40 (2H, m), 2.45 (2H, m), 2.77 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13.5, 5 Hz), 3.01-3.23 (3H, m), 3.94 (1H, m), 4.00 (2H, q, J=7 Hz), 4.28 (1H, dt, J=10, 7.5 Hz), 4.61 (1H, m), 4.68 (1H, m), 5.06 (1H, ddd, J=10, 10, 5 Hz), 6.32 (1H, d, J=10 Hz), 6.44 (1H, d, J=10 Hz), 6.80 (2x1H, d, J=8.7 Hz), 7.11 (2x1H, d, J=8.7 Hz), 7.14-7.31 (6H, m), 9.74 (1H, t, J=1.5 Hz);

MASS (ES+): m/e 563.49.

Preparation 538

Compound (538) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.30-1.85 (4H, m), 1.39 (3x3H, s), 2.54 (1H, m), 2.72 (1H, dd, J=12.8, 9.5 Hz), 2.85-3.02 (2H, m), 3.09 (1H, dd, J=14, 7 Hz), 3.48 (1H, m), 4.39 (1H, m), 4.90 (1H, m), 5.00 (1H, m), 5.10 (1H, d, J=12.5 Hz), 5.18 (1H, d, J=12.5 Hz), 6.63 (1H, brd, J=8.5 Hz), 7.12-7.40 (16H, m);

MASS (ES+): m/e 600.49.

10 Preparation 539

Compound (539) was obtained in a manner similar to Preparation 15.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.44-2.20 (4H, m), 2.66-2.90 (6H, m), 4.45 (1H, m), 4.72 (1H, m), 4.96 (1H, d, J=12 Hz), 5.02 (1H, m), 5.16 (1H, d, J=12 Hz), 7.01-7.50 (15H, m), 7.84-8.32 (3H, m);

MASS (ES+): m/e 500.50.

Preparation 540

Compound (540) was obtained in a manner similar to Preparation 16.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.20-1.95 (10H, m), 1.43 (3x3H, s), 2.60 (1H, m), 2.72-3.13 (4H, m), 3.52 (1H, m), 4.04 (1H, m), 4.20-4.34 (3H, m), 4.72 (1H, m), 4.88 (1H, m), 5.10 (1H, d, J=12.2 Hz), 5.13 (1H, m), 5.17 (1H, d, J=12.2 Hz), 6.72-6.83 (2H, m), 7.13-7.39 (15H, m), 7.42 (2x1H, dd, J=7.5, 7.5 Hz), 7.55 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES+): m/e 833.44.

Preparation 541

Compound (541) was obtained in a manner similar to Preparation 17.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.18-2.14 (10H, m), 2.66 (1H, m), 2.80-3.16 (4H, m), 3.69 (1H, m), 4.04 (1H, m), 4.20-4.34 (3H, m), 4.68-4.86 (2H, m), 5.28 (1H, brd, J=7.5 Hz), 6.92 (1H, brd, J=6 Hz), 7.08-7.31 (10H, m), 7.43 (2x1H, dd, J=7.5, 7.5 Hz), 7.49 (1H, brd, J=10 Hz), 7.55 (1H, m), 8.02 (2x1H, dd, J=7.5, 1.5 Hz);

35 MASS (ES+): m/e 743.43.

Preparation 542

Compound (542) was obtained in a manner similar to Preparation 18.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10-1.97 (10H, m), 2.72-3.16 (5H, m), 3.66 (1H, m), 4.05-4.30 (4H, m), 4.60 (1H, m), 5.12 (1H, m), 7.10-7.36 (10H, m), 7.40 (2x1H, dd, J=7.5, 7.5 Hz), 7.52 (1H, dd, J=7.5, 7.5 Hz), 7.94-8.38 (4H, m), 8.03 (2x1H, d, J=7.5 Hz);

MASS (ES<sup>+</sup>): m/e 643.53.

#### Preparation 543

Compound (543) was obtained in a manner similar to Preparation 76.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.32-1.54 (2H, m), 1.57-1.95 (6H, m), 2.12-2.38 (2H, m), 2.84 (1H, dd, J=14, 7 Hz), 2.88 (1H, dd, J=13.5, 5 Hz), 3.08 (1H, m), 3.14-3.26 (2H, m), 3.94 (1H, m), 4.28 (2H, t, J=6.5 Hz), 4.29 (1H, m), 4.62 (1H, dd, J=8, 2.5 Hz), 4.75 (1H, m), 5.07 (1H, ddd, J=10, 10, 5 Hz), 6.35 (1H, d, J=10 Hz), 6.48 (1H, d, J=10 Hz), 7.13-7.31 (11H, m), 7.44 (2x1H, dd, J=7.5, 7.5 Hz), 7.56 (1H, m), 8.03 (2x1H, dd, J=7.5, 1.5 Hz);

MASS (ES<sup>+</sup>): m/e 625.28.

#### Preparation 544

Compound (544) was obtained in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.20-1.91 (10H, m), 2.20 (1H, m), 2.31 (1H, m), 2.84 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13.5, 5 Hz), 3.08 (1H, m), 3.18 (1H, dd, J=13.5, 10.5 Hz), 3.21 (1H, dd, J=14, 9 Hz), 3.62 (2H, t, J=6.5 Hz), 3.94 (1H, m), 4.28 (1H, dt, J=10, 7.5 Hz), 4.62 (1H, dd, J=8, 2.5 Hz), 4.74 (1H, m), 5.06 (1H, ddd, J=10.5, 10, 5 Hz), 6.48 (1H, d, J=10 Hz), 6.52 (1H, d, J=10 Hz), 7.13-7.34 (11H, m);

MASS (ES<sup>+</sup>): m/e 521.

#### Preparation 545

Compound (545) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 302.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.46-1.90 (6H, m), 2.20 (1H, m), 2.32 (1H, m), 2.44 (2H, m), 2.79-2.92 (2H, m), 3.08 (1H, m), 3.13-3.27 (2H, m), 3.94 (1H, m), 4.28 (1H, dt, J=10.2, 7.3 Hz), 4.62 (1H, dd, J=8, 2 Hz), 4.74 (1H, m), 5.06 (1H, ddd, J=10, 10, 5 Hz), 6.38 (1H, d, J=10 Hz), 6.47 (1H, d, J=10 Hz), 7.14-7.33 (11H, m), 9.73 (1H, t, J=1 Hz);

MASS (ES+): m/e 519.

Preparation 546

Compound (546) was obtained in a manner similar to Preparation 16.

5  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.64-0.90 (6H, m), 1.12-2.00 (13H, m), 2.16 (1H, m), 2.46 (1H, m), 2.93-3.23 (5H, m), 3.85 (1H, m), 4.22 (2H, t,  $J=6.5$  Hz), 4.30-4.64 (3H, m), 4.82 (2/3H, m), 5.02-5.23 (4+2/3H, m), 5.34 (2/3H, brd,  $J=7.5$  Hz), 5.62 (1/3H, br), 6.34-6.60 (2H, m), 7.11-7.48 (17H, m), 7.55 (1H, m), 7.96-8.04 (2H, m);

10 MASS (ES+): m/e 847.48.

Preparation 547

Compound (547) was obtained in a manner similar to Preparation 17.

15  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.60-2.23 (21H, m), 2.46-2.68 (2H, m), 3.16 (1H, m), 3.46 (1H, m), 4.16-4.36 (2H, m), 4.41-4.68 (3H, m), 4.81 (1H, m), 7.14-7.72 (8H, m), 7.99 (2x1H, dd,  $J=7.5$ , 1.5 Hz);

MASS (ES+): m/e 623.57.

Preparation 548

20 Compound (548) was obtained in a manner similar to Preparation 76.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.72 (3H, m), 0.78 (3H, d,  $J=6.3$  Hz), 1.03-1.54 (6H, m), 1.58-1.98 (8H, m), 2.45 (1H, m), 2.70 (1H, m), 2.87 (1H, dd,  $J=13.7$ , 6.0 Hz), 3.24 (1H, dd,  $J=13.7$ , 9.8 Hz), 4.31 (2H, t,  $J=6.5$  Hz), 4.44-4.70 (4H, m), 4.86 (1H, m), 5.99 (1H, br), 6.07 (1H, br), 25 6.27 (1H, d,  $J=10.7$  Hz), 7.13-7.30 (5H, m), 7.43 (2x1H, dd,  $J=7.5$ , 7.5 Hz), 7.56 (1H, m), 8.02 (2x1H, dd,  $J=7.5$ , 1.5 Hz);

MASS (ES+): m/e 605.55.

Preparation 549

30 Compound (549) was obtained in a manner similar to Preparation 77.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.72 (3H, m), 0.78 (3H, d,  $J=6$  Hz), 1.02-1.96 (14H, m), 2.46 (1H, m), 2.75 (1H, m), 2.88 (1H, dd,  $J=13.5$ , 6 Hz), 3.25 (1H, dd,  $J=13.5$ , 10 Hz), 3.63 (2H, t,  $J=6$  Hz), 4.46-4.71 (4H, m), 4.89 (1H, m), 6.15 (1H, br), 6.29 (1H, br), 6.41 (1H, d,  $J=10.5$  Hz), 35 7.14-7.35 (5H, m);

MASS (ES+): m/e 501.60.

Preparation 550

Compound (550) was obtained in a manner similar to Preparation 78. The obtained compound was used in Example 305.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, m), 0.79 (3H, d, J=6.7 Hz), 1.08 (1H, m), 1.18-1.96 (11H, m), 2.39-2.56 (3H, m), 2.76 (1H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.25 (1H, dd, J=13.5, 10 Hz), 4.46-4.70 (4H, m), 4.87 (1H, m), 6.04-6.22 (2H, m), 6.31 (1H, d, J=10.5 Hz), 7.14-7.32 (5H, m), 9.76 (1H, s);

MASS (ES<sup>+</sup>): m/e 499.60.

10 Preparation 551

A solution of Compound (289) (300 mg) in a mixture of piperidine (1.2 ml) and N,N-dimethylformamide (4.8 ml) was stirred at ambient temperature for three hours. The mixture was concentrated in vacuo and the residue was purified by flash chromatography using ethyl acetate as a solvent to give the objective Compound (551) (275 mg) as a pale yellow oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.34-1.98 (8H, m), 2.07-2.23 (2H, m), 2.24-2.42 (2H, m), 2.83 (1H, dd, J=13.6, 5.9 Hz), 3.13 (1H, dd, J=13.6, 9.9 Hz), 3.19-3.34 (1H, m), 3.62 (2H, brs), 3.80-3.90 (1H, m), 4.18-4.29 (1H, m), 4.31 (2H, t, J=6.4 Hz), 4.67 (1H, brd, J=6.6 Hz), 5.11 (1H, dt, J=10.1, 5.9 Hz), 5.90 (1H, s), 6.60 (2H, d, J=8.4 Hz), 7.01 (2H, d, J=8.4 Hz), 7.18 (1H, d, J=10.3 Hz), 7.39-7.62 (4H, m), 7.99-8.06 (2H, m);

MASS (ES<sup>+</sup>): m/e 592.46 (M+1).

25 Preparation 552

To a stirred solution of the Compound (551) (540 mg) in pyridine (4 ml) was added methanesulfonyl chloride (110 mg) in an ice bath. The resulting mixture was stirred at the same temperature for two hours. The mixture was concentrated in vacuo and the residue was extracted with ethyl acetate, washed with water, 5% (w/v) potassium hydrogen sulfate, saturated aqueous sodium bicarbonate solution and brine. The organic layer was dried over magnesium sulfate, filtered and concentrated in vacuo. The residue was purified by flash chromatography using ethyl acetate as a solvent to give the objective Compound (552) (538 mg) as a pale yellow amorphous solid. The obtained compound was used in Example 90.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 1.29 (3H, s), 1.35-2.00 (8H, m), 2.06-2.41 (4H, m), 2.96 (1H, dd, J=13.9, 6.6 Hz), 2.99 (3H, s), 3.21 (1H, dd, J=13.9, 9.5 Hz), 3.26-3.36 (1H, m), 3.79-3.92 (1H, m), 4.20-4.32 (1H, m), 4.32 (2H, t, J=6.4 Hz), 4.70 (1H, brd, J=7.3 Hz), 5.09-5.22 (1H, m), 5.97 (1H, s), 6.51 (1H, s), 7.10 (1H, d, J=10.0 Hz), 7.13 (2H, d, J=8.8 Hz), 7.23 (2H, d, J=8.8 Hz), 7.40-7.49 (2H, m), 7.52-7.66 (2H, m), 8.00-8.07 (2H, m);  
MASS (ES<sup>+</sup>): m/e 670.53 (M+1).

#### Preparation 553

10 To a stirred solution of Compound (551) (260 mg) in pyridine (2 ml) was added acetic anhydride (1 ml) followed by a catalytic amount of 4-(dimethylamino)pyridine at ambient temperature, the resulting mixture was stirred at the same temperature for one hour. The volatiles were removed under reduced pressure and the residue was  
15 purified by flash chromatography using ethyl acetate then 5% methanol/ethyl acetate (v/v) as a solvent mixture to give the objective Compound (553) (260 mg) as a pale yellow amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.36-1.98 (8H, m), 2.06-2.24 (2H, m), 2.16 (3H, s), 2.25-2.41 (2H, m), 2.91  
20 (1H, dd, J=13.5, 5.7 Hz), 3.20 (1H, dd, J=13.5, 9.9 Hz), 3.21-3.34 (1H, m), 3.78-3.90 (1H, m), 4.18-4.30 (1H, m), 4.31 (2H, d, J=6.6 Hz), 4.66 (1H, brd, J=7.0 Hz), 5.14 (1H, dt, J=9.9, 5.9 Hz), 5.89 (1H, s), 7.12 (1H, d, J=9.9 Hz), 7.18 (2H, d, J=8.4 Hz), 7.40 (2H, d, J=8.4 Hz), 7.42-7.48 (2H, m), 7.50-7.60 (2H, m), 7.98-8.07 (2H, m);  
25 MASS (ES<sup>+</sup>): m/e 634.73.

#### Example 1

To a stirred solution of dimethyl (3R)-tert-butyl dimethylsilyloxy-2-oxobutylphosphonate (812 mg) in water and tetrahydrofuran (1:40) (7.5 ml) was added barium hydroxide octahydrate  
30 (482 mg) in one portion. The mixture was stirred at ambient temperature for 30 minutes. To the mixture was added a solution of Compound C1-3 (980 mg) in water and tetrahydrofuran (1:40) (1.5 ml once, 1 ml twice), and stirred for 1 hour. 10% Aqueous citric acid solution (50 ml) was added to the mixture to quench the reaction,  
35 stirred for 15 minutes under ice-cooling, and extracted with ethyl acetate (300 ml). The organic layer was washed with 10% citric acid

(50 ml), water (50 ml) and brine (50 ml), dried over sodium sulfate and evaporated in vacuo. The residue was purified by flash column chromatography (eluting with ethyl acetate/hexane = 2:3 to 1:1 v/v) to give Compound E1 as a white foam (852 mg).

- 5  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, s), 1.09 (9H, s), 1.22 (3H, d,  $J=7.0$  Hz), 1.28 (3H, s), 1.37-1.51 (2H, m), 1.54-1.89 (4H, m), 2.09-2.37 (6H, m), 2.89 (1H, dd,  $J=14.0$ , 6.2 Hz), 3.18 (1H, dd,  $J=14.0$ , 9.9 Hz), 3.19-3.29 (1H, m), 3.80-3.91 (1H, m), 4.15-4.28 (1H, m), 4.27 (1H, q,  $J=7.0$  Hz), 4.63-4.70 (1H, m), 5.02 (2H, s), 5.06-5.19 (1H, m), 5.84  
10 (1H, s), 6.61 (1H, d,  $J=15.4$  Hz), 6.80-6.89 (1H, m), 6.88 (2H, d,  $J=8.5$  Hz), 7.10-7.15 (1H, m), 7.14 (2H, d,  $J=8.5$  Hz), 7.28-7.49 (11H, m), 7.51 (1H, d,  $J=10.7$  Hz), 7.55-7.69 (4H, m);  
MASS (ES+): m/e 885.56 (M+).

Example 2

- 15 Compound E2 was obtained in a manner similar to Example 1.

- $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=6.7$  Hz), 1.09 (9H, s), 1.23 (3H, d,  $J=6.5$  Hz), 1.28 (3H, s), 1.35-1.53 (2H, m), 1.62-1.90 (3H, m), 2.09-2.38 (7H, m), 2.89 (1H, dd,  $J=13.5$ , 5.8 Hz), 3.18 (1H, dd,  $J=13.5$ , 9.9 Hz), 3.21-3.31 (1H, m), 3.81-3.92 (1H, m), 4.15-4.27 (1H, m), 4.27  
20 (1H, q,  $J=6.5$  Hz), 4.67 (1H, brd,  $J=5.6$  Hz), 5.03 (2H, s), 5.08-5.19 (1H, m), 5.79 (1H, s), 6.61 (1H, d,  $J=15.8$  Hz), 6.81-6.92 (1H, m), 6.88 (2H, d,  $J=8.8$  Hz), 7.09-7.17 (1H, m), 7.14 (2H, d,  $J=8.8$  Hz), 7.30-7.46 (11H, m), 7.50 (1H, d,  $J=10.7$  Hz), 7.57-7.62 (2H, m), 7.63-7.69 (2H, m);  
25 MASS (ES+): m/e 885.45 (M+).

Example 3

- To a solution of the Compound E1 (86.9 ml) in methanol (3 ml),  
Pd-BaSO<sub>4</sub> (56.2 mg) was added and stirred for 1.25 hours under hydrogen  
atmosphere. The catalyst was filtered through a pad of Celite® and  
30 the solvent was evaporated under reduced pressure. The residue was  
purified by preparative thin layer chromatography to give Compound E3  
as an oil (74.7 mg).

- $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=7.3$  Hz), 1.10 (9H, s), 1.26 (3H, d,  $J=6.6$  Hz), 1.10-1.36 (6H, m), 1.27 (3H, s), 1.40-1.65 (3H, m),  
35 1.67-1.85 (4H, m), 2.08-2.27 (2H, m), 2.27-2.40 (2H, m), 2.49 (2H, ddd,  $J=9.2$ , 7.0, 1.5 Hz), 2.88 (1H, dd,  $J=13.8$ , 5.9 Hz), 3.18 (1H, dd,

J=13.8, 9.9 Hz), 3.18-3.30 (1H, m), 3.81-3.92 (1H, m), 4.14-4.24 (2H, m), 4.18 (1H, d, J=5.8 Hz), 5.02 (2H, s), 5.13 (1H, ddd, J=16.1, 9.9, 6.2 Hz), 5.84 (1H, s), 6.88 (2H, d, J=8.8 Hz), 7.07 (1H, d, J=10.3 Hz), 7.15 (2H, d, J=8.4 Hz), 7.25-7.45 (11H, m), 7.56 (1H, d, J=10.38 Hz),  
5 7.55-7.68 (4H, m).

#### Example 4

To a solution of the Compound E1 in methanol-dioxane mixture (1:1) (20 ml) was added 10% palladium on carbon (300 mg) and the mixture was shaken under an atmosphere of hydrogen (4 atm) at ambient  
10 temperature for 20 hours. The mixture was filtered through a pad of Celite® and the filtrate was purified by flash chromatography (eluting with ethyl acetate/hexane = 1:1 to 2:2 v/v) to give Compound E4 as a colorless amorphous compound (610 mg).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.14-  
15 1.56 (6H, m), 1.19 (3H, d, J=6.8 Hz), 1.28 (3H, s), 1.69-1.88 (4H, m), 2.07-2.24 (2H, m), 2.24-2.37 (2H, m), 2.45-2.56 (2H, m), 2.88 (1H, dd, J=13.5, 6.3 Hz), 3.16 (1H, dd, J=13.5, 9.8 Hz), 3.20-3.31 (1H, m), 3.77-3.89 (1H, m), 4.11-4.20 (1H, m), 4.18 (1H, q, J=6.8 Hz), 4.67 (1H, brd, J=6.8 Hz), 5.06-5.18 (1H, m), 5.10 (1H, s), 5.89 (1H, s), 6.73  
20 (2H, d, J=8.4 Hz), 7.05-7.10 (1H, m), 7.09 (2H, d, J=8.4 Hz), 7.32-7.48 (6H, m), 7.53-7.70 (5H, m);

MASS (ES<sup>+</sup>): m/e 797.55 (M<sup>+</sup>).

#### Example 5

Compound E5 was obtained from the Compound E2 in a manner  
25 similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.19 (3H, d, J=6.7 Hz), 1.21-1.61 (7H, m), 1.28 (3H, s), 1.69-1.88 (3H, m),  
2.08-2.24 (2H, m), 2.25-2.38 (2H, m), 2.51 (2H, t, J=6.8 Hz), 2.89 (1H, dd, J=13.5, 6.2 Hz), 3.16 (1H, dd, J=13.5, 9.6 Hz), 3.21-3.31 (1H, m),  
30 3.77-3.90 (1H, m), 4.08-4.24 (2H, m), 4.67 (1H, brd, J=5.9 Hz), 5.05-5.18 (1H, m), 5.20 (1H, s), 5.85 (1H, s), 7.04-7.10 (1H, m), 7.09 (2H, d, J=8.5 Hz), 7.32-7.48 (6H, m), 7.53-7.68 (5H, m);

MASS (ES<sup>+</sup>): m/e 797.57 (M).

#### Example 6

35 To a stirred solution of the Compound E3 (74.7 mg) in tetrahydrofuran (3 ml) was added tetrabutylammonium fluoride (1.0M in

tetrahydrofuran, 0.1 ml) at ambient temperature and the mixture was stirred for 40 minutes at the same temperature. The reaction mixture was diluted with water (10 ml) and the organic layer was extracted with ethyl acetate (5 ml, twice). The combined organic layer was washed with brine (5 ml), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by preparative thin layer chromatography (chloroform : methanol = 10:1 v/v) to give Compound E6 (51.6 mg) as a colorless oil.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.20-1.40 (4H, m), 1.28 (3H, s), 1.37 (3H, d, J=7.0 Hz), 1.56-1.70 (2H, m), 1.70-1.88 (2H, m), 2.08-2.24 (2H, m), 2.25-2.58 (4H, m), 2.89 (1H, dd, J=13.6, 5.9 Hz), 3.18 (1H, dd, J=13.6, 9.9 Hz), 3.19-3.30 (1H, m), 3.61 (1H, d, J=4.4 Hz), 3.80-3.90 (1H, m), 4.15-4.28 (2H, m), 4.68 (6.6H, d), 5.02 (2H, s), 5.15 (1H, ddd, J=16.1, 9.9, 6.2 Hz), 5.89 (1H, s), 6.88 (2H, d, J=8.8 Hz), 7.10-7.18 (3H, m), 7.25-7.45 (5H, m), 7.54 (1H, d, J=10.3 Hz);

MASS(ES<sup>+</sup>): m/e 648.35 (M+1).

#### Example 7

Compound E7 was obtained from the Compound E5 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=6.9 Hz), 1.22-1.69 (7H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.1 Hz), 1.70-1.88 (3H, m), 2.07-2.24 (2H, m), 2.24-2.36 (2H, m), 2.88 (1H, dd, J=13.4, 5.5 Hz), 3.15 (1H, dd, J=13.4, 9.4 Hz), 3.20-3.32 (1H, m), 3.57 (1H, d, J=4.6 Hz), 3.77-3.89 (1H, m), 4.13-4.28 (2H, m), 4.68 (1H, brd, J=5.8 Hz), 5.05-5.18 (1H, m), 5.40 (1H, s), 5.89 (1H, s), 6.73 (2H, d, J=8.0 Hz), 7.09 (2H, d, J=8.0 Hz), 7.12 (1H, d, J=10.0 Hz), 7.55 (1H, d, J=10.2 Hz);

MASS (ES<sup>+</sup>): m/e 559.41 (M+1).

#### Example 8

Compound E8 was obtained from the Compound E4 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.1 Hz), 1.21-1.41 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.53-1.69 (3H, m), 1.70-1.89 (3H, m), 2.06-2.23 (2H, m), 2.24-2.38 (2H, m), 2.39-2.55 (2H, m), 2.88 (1H, dd, J=13.5, 5.8 Hz), 3.15 (1H, dd, J=13.5, 9.6 Hz), 3.19-3.31 (1H, m),

3.57 (1H, d, J=4.7 Hz), 3.77-3.89 (1H, m), 4.07-4.29 (2H, m), 4.67 (1H, br d, J=6.5 Hz), 5.06-5.18 (1H, m), 5.29 (1H, s), 15.93 (1H, s), 6.73 (2H, d, J=8.5 Hz), 7.09 (2H, d, J=8.5 Hz), 7.12 (1H, d, J=10.0 Hz), 7.55 (1H, d, J=10.3 Hz);

5 MASS (ES+): m/e 559.31 (M+1).

#### Example 9

Compound E9 was obtained from the Compound (81) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.09 (3x3H, s),  
10 1.22 (3H, d, J=7 Hz), 1.28 (3H, s), 1.38-1.52 (2H, m), 1.56-1.90 (4H, m), 2.08-2.40 (6H, m), 2.89 (1H, dd, J=14, 6 Hz), 3.18 (1H, dd, J=14, 10 Hz), 3.26 (1H, m), 3.77 (3H, s), 3.86 (1H, m), 4.21 (1H, m), 4.26 (1H, q, J=7 Hz), 4.66 (1H, m), 5.14 (1H, ddd, J=10, 10, 6 Hz), 5.84 (1H, s), 6.62 (1H, brd, J=16 Hz), 6.81 (2x1H, d, J=8.5 Hz), 6.84 (1H, dt, J=16, 7 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.29-7.45 (6H, m), 7.51 (1H, d, J=10 Hz), 7.55-7.68 (4H, m);

MASS (ES-): m/e 807.

#### Example 10

20 Compound E10 was obtained from the Compound (80) in a manner similar to Example 2.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.8 Hz), 1.21 (9H, s), 1.26 (3H, d, J=6.9 Hz), 1.63 (3H, s), 1.70-1.58 (4H, m), 1.71-1.79 (3H, m), 2.09-2.39 (6H, m), 2.89 (1H, dd, J=13.8, 5.7 Hz), 3.18 (1H, dd, J=13.8, 9.6 Hz), 3.22-3.31 (1H, m), 3.77 (3H, s), 3.79-3.92 (1H, m), 4.18-4.27  
25 (1H, m), 4.27 (1H, q, J=6.9 Hz), 5.13 (1H, ddd, J=9.9, 9.9, 5.7 Hz), 5.84 (1H, s), 6.61 (1H, d, J=15.3 Hz), 6.81 (2H, d, J=8.7 Hz), 6.86 (1H, dt, J=15.3, 6.9 Hz), 7.15 (2H, d, J=8.7 Hz), 7.31-7.48 (5H, m), 7.51 (1H, d, J=10.5 Hz), 7.57-7.69 (5H, m);

MASS (ES+): m/e 809.48 (M).

#### 30 Example 11

Compound E11 was obtained from the Compound E9 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=7 Hz), 1.20-1.30 (4H, m), 1.28 (3H, s), 1.40-1.51 (2H, m), 1.60 (1H, m), 1.68-1.88 (3H, m), 2.09-2.24 (2H, m), 2.25-2.38 (2H, m), 2.51 (2H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5,

10 Hz), 3.26 (1H, m), 3.85 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7 Hz), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.85 (1H, s), 6.81 (2x1H, d, J=8.5 Hz), 7.08 (1H, d, J=10 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.33-7.48 (6H, m), 7.56 (1H, d, J=10 Hz), 7.59-7.68 (4H, m);

5 MASS (ES+): m/e 811.

Example 12

Compound E12 was obtained from the Compound E10 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 1.10 (9H, s), 1.16-1.32 (11H, m), 1.18 (3H, d, J=6.6 Hz), 1.38-1.51 (1H, m), 1.61 (3H, s), 1.68-1.88 (2H, m), 2.08-2.24 (2H, m), 2.25-2.39 (2H, m), 2.50 (2H, t), 2.89 (1H, dd, J=13.5, 6.0 Hz), 3.18 (1H, dd, J=13.5, 9.9 Hz), 3.23-3.30 (1H, m), 3.77 (3H, s), 3.81-3.90 (1H, m), 4.13-4.23 (1H, m), 4.18 (1H, q, J=6.6 Hz), 4.64-4.69 (1H, m), 5.13 (1H, ddd, J=9.9, 9.9, 6.3 Hz), 5.84 (1H, s), 6.81 (2H, d, J=8.7 Hz), 7.08 (1H, d, J=9.9 Hz), 7.15 (2H, d, J=8.7 Hz), 7.33-7.48 (6H, m), 7.55 (1H, d, J=10.2 Hz);  
15 MASS (ES+): m/e 811.49.

Example 13

20 Compound E13 was obtained from the Compound E11 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.20-1.40 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.69 (3H, m), 1.70-1.90 (3H, m), 2.08-2.23 (2H, m), 2.26-2.56 (4H, m), 2.89 (1H, dd, J=14, 6 Hz), 3.18 (1H, dd, J=14, 10 Hz), 3.26 (1H, m), 3.56 (1H, d, J=5 Hz), 3.86 (1H, m), 4.14-4.30 (2H, m), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.87 (1H, s), 6.81 (2x1H, d, J=9 Hz), 7.12 (1H, d, J=11 Hz), 7.14 (2x1H, d, J=9 Hz), 7.53 (1H, d, J=10 Hz);  
25 MASS (ES-): m/e 571;

$[\alpha]_D^{25} = -116.5^\circ$  (c=0.31, CHCl<sub>3</sub>).

30 Example 14

Compound E14 was obtained from the Compound E12 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=6.9 Hz), 1.23-1.40 (2H, m), 1.38 (3H, d, J=7.2 Hz), 1.55-1.90 (6H, m), 1.64 (3H, s), 2.05-2.58 (6H, m), 2.88 (1H, dd, J=13.5, 6.0 Hz), 3.18 (1H, dd, J=13.5, 9.9 Hz), 3.21-3.30 (1H, m), 3.55 (1H, d, J=4.8 Hz), 3.78 (3H, s), 3.80-3.90 (1H,

m), 4.16-4.28 (1H, m), 4.19 (1H, q, 7.2 Hz), 4.64-4.70 (1H, m), 5.13 (1H, ddd, J=9.9, 9.9, 6.0 Hz), 5.89 (1H, s), 6.81 (2H, d, J=8.4 Hz), 7.12 (1H, d, J=9.3 Hz), 7.14 (2H, d, J=8.4 Hz), 7.53 (1H, d, J=10.2 Hz);

5 MASS (ES+): m/e 573.49 (M+1).

#### Example 15

Compound E15 was obtained from the Compound (84) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.0 Hz), 1.10 (9H, s), 1.23 (3H, d, J=6.9 Hz), 1.29 (3H, s), 1.36-1.55 (2H, m), 1.63-1.90 (4H, m), 2.07-2.39 (6H, m), 2.95 (1H, dd, J=13.9, 7.4 Hz), 3.21 (1H, dd, J=13.9, 8.7 Hz), 3.22-3.34 (1H, m), 3.80-3.91 (1H, m), 4.18-4.29 (1H, m), 4.28 (1H, q, J=6.9 Hz), 4.68 (1H, brd, J=7.1 Hz), 5.08-5.20 (1H, m), 5.83 (1H, s), 6.62 (1H, d, J=15.7 Hz), 6.82-6.98 (1H, m), 6.97 (2H, t, J=8.7 Hz), 7.09 (1H, d, J=10.6 Hz), 7.20 (2H, dd, J=8.7, 5.4 Hz), 7.29-7.48 (6H, m), 7.55 (1H, d, J=10.6 Hz), 7.56-7.69 (4H, m);  
15 MASS (ES+): m/e 797.59 (M+1).

#### Example 16

Compound E16 was obtained from the Compound E15 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of Pd-BaSO<sub>4</sub>.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.16-1.32 (3H, m), 1.18 (3H, d, J=6.7 Hz), 1.28 (3H, s), 1.38-1.62 (4H, m), 1.72-1.88 (3H, m), 2.09-2.38 (4H, m), 2.46-2.55 (2H, m), 2.93 (1H, dd, J=13.2, 7.1 Hz), 3.20 (1H, dd, J=13.2, 8.7 Hz), 3.22-3.32 (1H, m), 3.79-3.89 (1H, m), 4.12-4.24 (1H, m), 4.19 (1H, q, J=6.7 Hz), 4.67 (1H, brd, J=5.4 Hz), 5.08-5.19 (1H, m), 5.83 (1H, s), 6.96 (2H, t, J=8.6 Hz), 7.04 (1H, d, J=10.2 Hz), 7.19 (2H, dd, J=8.6, 5.5 Hz), 7.32-7.48 (6H, m), 7.54-7.67 (5H, m);  
25  
30 MASS (ES+): m/e 799.52 (M).

#### Example 17

Compound E17 was obtained from the Compound E16 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.24-1.39 (6H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.2 Hz), 1.54-1.69 (1H, m), 1.71-1.89 (3H, m), 2.08-2.58 (6H, m), 2.93 (1H, dd, J=13.9, 6.3 Hz), 3.20 (1H, dd,

J=13.9, 9.6 Hz), 3.21-3.32 (1H, m), 3.55 (1H, d, J=4.7 Hz), 3.78-3.91 (1H, m), 4.14-4.29 (2H, m), 4.68 (1H, brd, J=5.8 Hz), 5.08-5.19 (1H, m), 5.87 (1H, s), 6.96 (2H, t, J=8.8 Hz), 7.07 (1H, d, J=10.4 Hz), 7.19 (2H, dd, J=8.8, 5.5 Hz), 7.56 (1H, d, J=10.7 Hz);

5 MASS (ES+): m/e 561.46 (M+1).

#### Example 18

Compound E18 was obtained from the Compound (87) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (9H, s), 1.22 (1H, d, J=7.2 Hz), 1.37-1.88 (15H, m), 2.12-2.38 (3H, m), 2.43-2.58 (2H, m), 2.95 (1H, dd, J=13.5, 6.0 Hz), 3.25 (1H, dd, J=13.5, 10.2 Hz), 3.28-3.13 (1H, m), 3.85-3.95 (1H, m), 4.22 (1H, dt, J=10.2, 7.8 Hz), 4.27 (1H, q, J=7.2 Hz), 4.64-4.69 (1H, m), 5.15 (1H, ddd, J=9.9, 9.9, 5.7 Hz), 6.16 (1H, s), 6.61 (1H, d, J=15.6 Hz), 6.87 (1H, dt, J=15.6, 6.9 Hz), 7.16-7.33 (5H, m), 7.33-7.48 (8H, m), 7.57-7.74 (4H, m);

15 MASS (ES+): m/e 791.60 (M).

#### Example 19

Compound E19 was obtained from the Compound E18 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of Pd-BaSO<sub>4</sub>.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.01-1.84 (17H, m), 1.18 (3H, d, J=6.9 Hz), 2.11-2.36 (2H, m), 2.41-2.58 (3H, m), 2.95 (1H, dd, J=10.5, 6.0 Hz), 3.15-3.26 (1H, m), 3.26 (1H, dd, J=10.5, 13.5 Hz), 3.84-3.94 (1H, m), 4.12 (1H, dt, J=6.9, 7.5 Hz), 4.18 (1H, q, J=6.9 Hz), 4.63-4.69 (1H, m), 5.14 (1H, ddd, J=9.6, 9.6, 6.0 Hz), 6.14 (1H, s), 7.13 (1H, d, J=10.2 Hz), 7.17-7.31 (4H, m), 7.32-7.49 (8H, m), 7.57-7.66 (4H, m);

25 MASS (ES+): m/e 793.57 (M).

#### Example 20

30 Compound E20 was obtained from the Compound E19 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.19-1.87 (17H, m), 1.38 (3H, d, J=7.2 Hz), 2.11-2.23 (1H, m), 2.24-2.39 (2H, m), 2.40-2.58 (2H, m), 2.95 (1H, dd, J=13.5, 6.0 Hz), 3.15-3.25 (1H, m), 3.25 (1H, dd, J=13.5, 10.2 Hz), 3.56 (1H, d, J=4.8 Hz), 3.86-3.95 (1H, m), 4.12 (1H, q, J=7.2 Hz), 4.28-4.12 (1H, m), 4.63-4.69 (1H, m), 5.15 (1H, ddd, J=10.2, 10.2, 6.0

Hz), 6.18 (1H, s), 7.14-7.34 (6H, m), 7.43 (1H, d, J=10.2 Hz);

MASS (ES+): m/e 555.41 (M+1).

#### Example 21

Compound 21 was obtained from the Compound (90) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.812 (3H, t, J=7.2 Hz), 1.10 (6H, s), 1.11 (3H, s), 1.27 (3H, s), 1.37-1.91 (8H, m), 2.08-2.39 (6H, m), 3.06 (1H, dd, J=14.7, 6.9 Hz), 3.25-3.36 (1H, m), 3.27 (1H, dd, J=14.7, 8.7 Hz), 3.80-3.89 (1H, m), 4.18-4.31 (1H, m), 4.26 (2H, t, J=6.6 Hz), 4.66-4.71 (1H, m), 5.13-5.23 (1H, m), 5.89 (1H, s), 6.62 (1H, d, J=15.9 Hz), 6.87 (1H, dt, J=15.9, 6.9 Hz), 7.01 (1H, d, J=10.8 Hz), 7.30-7.49 (7H, m), 7.56-7.68 (8H, m);

MASS (ES+): m/e 804.62 (M+1).

#### Example 22

Compound E22 was obtained from the Compound E21 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of 5% Pd-BaSO<sub>4</sub>.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.807 (3H, t, J=6.9 Hz), 1.10 (9H, s), 1.28 (3H, s), 1.38-1.90 (11H, m), 2.06-2.39 (6H, m), 2.51 (2H, dt, J=7.2, 2.7 Hz), 3.06 (1H, dd, J=13.5, 7.5 Hz), 3.26-3.36 (1H, m), 3.27 (1H, dd, J=13.5, 9.0 Hz), 3.79-3.88 (1H, m), 4.19 (1H, dq, J=6.6, 2.7 Hz), 4.25 (1H, dt, J=13.8, 6.9 Hz), 4.66-4.71 (1H, m), 5.18 (1H, dt, J=9.6, 8.1 Hz), 5.87 (1H, s), 6.95 (1H, d, J=10.2 Hz), 7.32-7.49 (7H, m), 7.58-7.69 (7H, m), 7.58 (1H, d, J=9.0 Hz);

MASS (ES+): m/e 806.38 (M+1).

#### Example 23

Compound E23 was obtained from the Compound E22 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.811 (3H, t, J=7.5 Hz), 1.24-1.68 (11H, m), 1.38 (3H, d, J=7.2 Hz), 1.75-1.89 (3H, m), 2.06-2.57 (6H, m), 3.06 (1H, dd, J=14.1, 7.5 Hz), 3.26-3.36 (1H, m), 3.26 (1H, dd, J=14.1, 8.7 Hz), 3.79-3.88 (1H, m), 4.15-4.28 (2H, m), 4.65-4.71 (1H, m), 5.18 (1H, dt, J=8.4, 7.2 Hz), 5.90 (1H, s), 6.99 (1H, d, J=10.5 Hz), 7.33-7.39 (2H, m), 7.56-7.61 (2H, m), 7.63 (1H, d, J=10.2 Hz);

MASS (ES+): m/e 568.50 (M+1).

Example 24

Compound E24 was obtained from the Compound (93) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.2 Hz), 1.09 (5H, s), 1.10 (4H, s), 1.22 (3H, d, J=6.9 Hz), 1.28 (3H, s), 1.37-1.90 (8H, m), 1.39 (3H, t, J=6.9 Hz), 2.10-2.38 (4H, m), 2.88 (1H, dd, J=13.5, 5.7 Hz), 3.19 (1H, dd, J=13.5, 9.6 Hz), 3.12-3.30 (1H, m), 3.81-3.90 (1H, m), 3.99 (2H, q, J=6.9 Hz), 4.16-4.31 (2H, m), 4.64-4.69 (1H, m), 5.13 (1H, dt, J=9.6, 5.7 Hz), 5.85 (1H, s), 6.61 (1H, d, J=15.9 Hz), 6.79 (2H, d, J=8.4 Hz), 6.86 (1H, dt, J=15.9 Hz), 7.12-7.17 (1H, m), 7.13 (2H, d, J=8.4 Hz), 7.31-7.47 (5H, m), 7.50 (1H, d, J=10.2 Hz), 7.56-7.68 (5H, m);

MASS (ES<sup>+</sup>): m/e 823.64 (M+1).

Example 25

Compound E25 was obtained from the Compound E24 in a manner similar to Example 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.2 Hz), 1.11 (9H, s), 1.20 (3H, d, J=6.9 Hz), 1.20-1.65 (7H, m), 1.29 (3H, s), 1.40 (3H, t, J=6.9 Hz), 1.71-1.86 (3H, m), 2.09-2.24 (2H, m), 2.26-2.38 (2H, m), 2.52 (1H, dt, J=7.5, 2.1 Hz), 2.89 (1H, dd, J=13.5, 5.7 Hz), 3.13-3.31 (1H, m), 3.23 (1H, dd, J=13.5, 9.6 Hz), 3.81-3.90 (1H, m), 4.00 (1H, q, J=6.9 Hz), 4.19 (1H, dq, J=6.9, 2.1 Hz), 4.64-4.70 (1H, m), 5.14 (1H, dt, J=9.6, 5.7 Hz), 5.83 (1H, s), 6.80 (2H, d, J=8.7 Hz), 7.10 (1H, d, J=11.1 Hz), 7.14 (2H, d, J=8.7 Hz), 7.34-7.48 (5H, m), 7.55 (1H, d, J=10.5 Hz), 7.60-7.67 (5H, m);

MASS (ES<sup>+</sup>): m/e 825.65 (M+1).

Example 26

Compound E26 was obtained from the Compound E25 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=6.9 Hz), 1.20-1.42 (7H, m), 1.28 (3H, s), 1.39 (3H, t, J=7.2 Hz), 1.52-1.69 (3H, m), 1.71-1.87 (3H, m), 2.08-2.24 (2H, m), 2.26-2.39 (2H, m), 2.46 (2H, dt, J=11.7, 7.2 Hz), 2.88 (1H, dd, J=13.2, 5.7 Hz), 3.17 (1H, dd, J=13.2, 11.2 Hz), 3.22-3.30 (1H, m), 3.55 (1H, d, J=4.5 Hz), 3.81-3.90 (1H, m), 3.99 (2H, q, J=7.2 Hz), 4.14-4.28 (2H, m), 4.64-4.69 (1H, m), 5.13 (1H, dt, J=11.2, 5.7 Hz), 5.84 (1H, s), 7.08-7.16 (1H, m), 7.13 (2H, d, J=8.4

Hz), 7.52 (1H, d, J=10.5 Hz);

MASS (ES+): m/e 587.56 (M+1).

Example 27

Compound E27 was obtained from the Compound (96) in a manner  
5 similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7 Hz), 1.09 (3x3H, s), 1.22  
(3H, d, J=7 Hz), 1.26 (3H, s), 1.45 (2H, m), 1.65 (1H, m), 1.74-1.93  
(3H, m), 2.10-2.40 (6H, m), 3.11 (1H, dd, J=15, 8 Hz), 3.15 (1H, dd,  
J=15, 8 Hz), 3.40 (1H, m), 3.88 (1H, m), 4.21 (1H, m), 4.27 (1H, q,  
10 J=7 Hz), 4.69 (1H, m), 5.24 (1H, ddd, J=9, 8, 8 Hz), 5.80 (1H, s),  
6.62 (1H, d, J=16 Hz), 6.87 (1H, dt, J=16, 7 Hz), 6.96-7.13 (3H, m),  
7.15-7.27 (2H, m), 7.30-7.48 (6H, m), 7.52 (3H, d, J=9 Hz), 7.55-7.70  
(4H, m);

MASS (ES-): m/e 795.

15 Example 28

Compound E28 was obtained from the Compound (96) in a manner  
similar to Example 2.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7 Hz), 1.09 (3x3H, s), 1.22  
(3H, d, J=7 Hz), 1.26 (3H, s), 1.45 (2H, m), 1.65 (1H, m), 1.72-1.92  
20 (3H, m), 2.10-2.40 (6H, m), 3.11 (1H, dd, J=15, 8 Hz), 3.15 (1H, dd,  
J=15, 8 Hz), 3.40 (1H, m), 3.88 (1H, m), 4.21 (1H, m), 4.27 (1H, q,  
J=7 Hz), 4.70 (1H, dd, J=8, 2 Hz), 5.23 (1H, ddd, J=9, 8, 8 Hz), 5.78  
(1H, s), 6.61 (1H, d, J=16 Hz), 6.86 (1H, dt, J=16, 7 Hz), 6.96-7.12  
(3H, m), 7.15-7.28 (2H, m), 7.30-7.48 (6H, m), 7.52 (1H, d, J=9 Hz),  
25 7.55-7.69 (4H, m);

MASS (ES-): m/e 795.

Example 29

Compound E29 was obtained from the Compound (96) in a manner  
similar to Example 1 except that dimethyl (3R)-tert-  
30 butyldimethylsilyloxy-2-oxopentylphosphonate was used instead of  
dimethyl (3R)-tert-butyldimethylsilyloxy-2-oxobutylphosphonate.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7 Hz), 0.80 (3H, t, J=7 Hz),  
1.10 (3x3H, s), 1.26 (3H, s), 1.42 (2H, m), 1.55-1.70 (3H, m), 1.72-  
1.91 (3H, m), 2.10-2.41 (6H, m), 3.11 (1H, dd, J=14, 8 Hz), 3.15 (1H,  
35 dd, J=14, 8 Hz), 3.41 (1H, m), 3.89 (1H, m), 4.14 (1H, q, J=7 Hz),  
4.21 (1H, m), 4.69 (1H, m), 5.24 (1H, ddd, J=10, 8, 8 Hz), 5.78 (1H,

s), 6.55 (1H, d, J=16 Hz), 6.80 (1H, dt, J=16, 7 Hz), 6.97-7.12 (3H, m), 7.15-7.27 (2H, m), 7.29-7.47 (6H, m), 7.52 (1H, d, J=10 Hz), 7.55-7.67 (4H, m);

MASS (ES-): m/e 809.

5 Example 30

Compound E30 was obtained from the Compound E27 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of Pd-BaSO<sub>4</sub>.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7 Hz), 1.10 (3x3H, s), 1.15-1.34 (4H, m), 1.18 (3H, d, J=7 Hz), 1.45 (2H, m), 1.60 (1H, m), 1.72-1.92 (3H, m), 2.08-2.40 (4H, m), 2.50 (2H, m), 3.10 (1H, dd, J=15, 8 Hz), 3.15 (1H, dd, J=15, 7.5 Hz), 3.41 (1H, m), 3.87 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7 Hz), 4.69 (1H, m), 5.23 (1H, ddd, J=10, 8, 7.5 Hz), 5.80 (1H, s), 6.96-7.08 (3H, m), 7.15-7.27 (2H, m), 7.32-7.49 (6H, m), 7.55 (1H, d, J=10 Hz), 7.55-7.70 (5H, m);

MASS (ES-): m/e 797.

Example 31

Compound E31 was obtained from the Compound E30 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of Pd-BaSO<sub>4</sub>.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7 Hz), 1.10 (3x3H, s), 1.15-1.32 (4H, m), 1.18 (3H, d, J=7 Hz), 1.45 (2H, m), 1.60 (1H, m), 1.71-1.92 (3H, m), 2.09-2.40 (4H, m), 2.51 (2H, t, J=7 Hz), 3.10 (1H, dd, J=15, 8 Hz), 3.15 (1H, dd, J=15, 8 Hz), 3.40 (1H, m), 3.87 (1H, m), 4.18 (1H, q, J=7 Hz), 4.18 (1H, m), 4.69 (1H, m), 5.23 (1H, ddd, J=10, 8, 7.5 Hz), 5.79 (1H, s), 6.95-7.09 (3H, m), 7.14-7.28 (2H, m), 7.32-7.49 (6H, m), 7.55 (1H, d, J=10 Hz), 7.55-7.68 (6H, m);

MASS (ES-): m/e 797.

Example 32

Compound E32 was obtained from the Compound E29 in a manner similar to Example 3 except that 10% palladium on carbon was used instead of Pd-BaSO<sub>4</sub>.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7 Hz), 0.81 (3H, t, J=7 Hz), 1.11 (3x3H, s), 1.13-1.28 (4H, m), 1.26 (3H, s), 1.37 (2H, m), 1.49-1.67 (3H, m), 1.71-1.92 (3H, m), 2.08-2.49 (6H, m), 3.10 (1H, dd, J=15, 8 Hz), 3.15 (1H, dd, J=15, 7.5 Hz), 3.40 (1H, m), 3.87 (1H, m), 4.10

(1H, t, J=6 Hz), 4.17 (1H, m), 4.69 (1H, m), 5.23 (1H, ddd, J=9, 8, 7.5 Hz), 5.79 (1H, s), 6.96-7.08 (3H, m), 7.14-7.28 (2H, m), 7.32-7.47 (6H, m), 7.55 (1H, d, J=9 Hz), 7.55-7.66 (5H, m);  
MASS (ES-): m/e 811.

5 Example 33

Compound E33 was obtained from the Compound E30 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.5 Hz), 1.24-1.42 (4H, m), 1.26 (3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.70 (3H, m), 1.74-1.92 (3H, m), 2.08-2.58 (6H, m), 3.11 (1H, dd, J=15, 8 Hz), 3.15 (1H, dd, J=15, 7 Hz), 3.41 (1H, m), 3.58 (1H, d, J=5 Hz), 3.87 (1H, m), 4.13-4.30 (2H, m), 4.70 (1H, m), 5.24 (1H, ddd, J=10, 8, 7 Hz), 5.84 (1H, s), 6.97-7.12 (3H, m), 7.15-7.30 (2H, m), 7.54 (1H, d, J=10 Hz);

MASS (ES-): m/e 559;

15 MASS (ES+): m/e 561.

Example 34

Compound E34 was obtained from the Compound E31 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.5 Hz), 1.20-1.42 (4H, m), 1.26 (3H, s), 1.38 (3H, d, J=7 Hz), 1.53-1.73 (3H, m), 1.74-1.93 (3H, m), 2.09-2.59 (6H, m), 3.10 (1H, dd, J=15, 8 Hz), 3.15 (1H, dd, J=15, 7 Hz), 3.40 (1H, m), 3.56 (1H, d, J=5 Hz), 3.87 (1H, m), 4.14-4.29 (2H, m), 4.70 (1H, m), 5.24 (1H, ddd, J=10, 8, 7 Hz), 5.83 (1H, s), 6.96-7.13 (3H, m), 7.15-7.29 (2H, m), 7.54 (1H, d, J=10 Hz);

25 MASS (ES-): m/e 559.

Example 35

Compound E35 was obtained from the Compound E32 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7.5 Hz), 0.94 (3H, t, J=7.5 Hz), 1.17-1.40 (4H, m), 1.26 (3H, s), 1.50-1.78 (4H, m), 1.79-1.97 (4H, m), 2.08-2.40 (6H, m), 2.45 (2H, m), 3.10 (1H, dd, J=15, 7.5 Hz), 3.14 (1H, dd, J=15, 7.5 Hz), 3.40 (1H, m), 3.51 (1H, d, J=5 Hz), 3.87 (1H, m), 4.08-4.26 (2H, m), 4.70 (1H, m), 5.23 (1H, ddd, J=9, 7.5, 7.5 Hz), 5.85 (1H, s), 6.95-7.12 (3H, m), 7.14-7.31 (2H, m), 7.54 (1H, d, J=9 Hz);

MASS (ES-): m/e 573;

MASS (ES+): m/e 575.

Example 36

Compound E36 was obtained from the Compound (99) in a manner similar to Example 1.

5  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=7.3$  Hz), 1.09 (3x3H, s),  
1.22 (3H, d,  $J=7$  Hz), 1.28 (3H, s), 1.38–1.52 (2H, m), 1.64 (1H, m),  
1.70–1.91 (3H, m), 2.08–2.38 (6H, m), 2.94 (1H, dd,  $J=14$ , 6 Hz), 3.20  
(1H, dd,  $J=14$ , 9.5 Hz), 3.28 (1H, m), 3.86 (1H, m), 4.22 (1H, m), 4.27  
(1H, q,  $J=7$  Hz), 4.67 (1H, m), 5.14 (1H, ddd,  $J=10$ , 9.5, 6 Hz), 5.87  
10 (1H, s), 6.62 (1H, d,  $J=16$  Hz), 6.86 (1H, dt,  $J=16.7$  Hz), 7.08 (1H, d,  
 $J=10$  Hz), 7.16 (2x1H, d,  $J=8.5$  Hz), 7.24 (2x1H, d,  $J=8.5$  Hz), 7.31–  
7.48 (6H, m), 7.52–7.69 (5H, m);

MASS (ES+): m/e 813.

Example 37

15 Compound E37 was obtained from the Compound E36 in a manner similar to Example 3.

$^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=7$  Hz), 1.10 (3x3H, s), 1.18  
(3H, d,  $J=6.5$  Hz), 1.20–1.30 (4H, m), 1.28 (3H, s), 1.40–1.50 (2H, m),  
1.60 (1H, m), 1.72–1.89 (3H, m), 2.08–2.38 (4H, m), 2.51 (2H, m), 2,  
20 94 (1H, dd,  $J=14$ , 6 Hz), 3.20 (1H, dd,  $J=14$ , 10 Hz), 3.28 (1H, m),  
3.84 (1H, m), 4.19 (1H, q,  $J=6.5$  Hz), 4.19 (1H, m), 4.67 (1H, m),  
5.14 (1H, ddd,  $J=10$ , 10, 6 Hz), 5.87 (1H, s), 7.03 (1H, d,  $J=10.5$  Hz),  
7.17 (2x1H, d,  $J=9$  Hz), 7.24 (2x1H, d,  $J=9$  Hz), 7.33–7.50 (6H, m), 7,  
56–7.68 (5H, m);

25 MASS (ES+): m/e 815.

Example 38

Compound E38 was obtained from the Compound E37 in a manner similar to Example 6.

$^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=7.3$  Hz), 1.20–1.40 (4H, m),  
30 1.28 (3H, s), 1.38 (3H, d,  $J=7$  Hz), 1.55–1.70 (3H, m), 1.72–1.90 (3H,  
m), 2.08–2.58 (6H, m), 2.94 (1H, dd,  $J=14.6$  Hz), 3.20 (1H, dd,  $J=14$ ,  
10 Hz), 3.28 (1H, m), 3.56 (1H, d,  $J=5$  Hz), 3.85 (1H, m), 4.15–4.30  
(2H, m), 4.68 (1H, m), 5.14 (1H, ddd,  $J=10$ , 10, 6 Hz), 5.90 (1H, s),  
7.06 (1H, d,  $J=10$  Hz), 7.17 (2x1H, d,  $J=9$  Hz), 7.24 (2x1H, d,  $J=9$  Hz),  
35 7, 58 (1H, d,  $J=10$  Hz);

MASS (ES+): m/e 577;

$[\alpha]_D^{25} = -116.1^\circ$  (c=0.31, CHCl<sub>3</sub>).

Example 39

Compound E39 was obtained from the Compound (102) in a manner similar to Example 1.

5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.7 Hz), 0.91 (3H, t, J=7.3 Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.37-1.70 (4H, m), 1.71-1.92 (4H, m), 2.07-2.45 (6H, m), 2.97 (1H, dd, J=13.5, 5.8 Hz), 3.18-3.31 (2H, m), 3.83-3.95 (1H, m), 4.15-4.29 (1H, m), 4.27 (1H, q, J=6.9 Hz), 4.66 (1H, brd, J=6.9 Hz), 5.12-5.24 (1H, m), 5.79 (1H, s), 6.61  
10 (1H, d, J=15.6 Hz), 6.86 (1H, dt, J=15.6, 6.7 Hz), 7.13 (1H, d, J=9.9 Hz), 7.17-7.29 (5H, m), 7.30-7.45 (6H, m), 7.49 (1H, d, J=10.6 Hz); 7.56-7.69 (4H, m);  
MASS (ES+): m/e 793.32 (M+1).

Example 40

15 Compound E40 was obtained from the Compound E39 in a manner similar to Example 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.3 Hz), 0.92 (3H, t, J=7.3 Hz), 1.11 (9H, s), 1.15-1.35 (4H, m), 1.19 (3H, t, J=6.6 Hz), 1.37-1.69 (5H, m), 1.70-1.91 (3H, m), 2.11-2.46 (4H, m), 2.52 (2H, dt, J=7.0, 2.5 Hz), 2.97 (1H, dd, J=13.5, 6.3 Hz), 3.18-3.31 (2H, m),  
20 3.82-3.96 (1H, m), 4.16-4.26 (1H, m), 4.19 (1H, q, J=6.5 Hz), 4.67 (1H, d, J=5.9 Hz), 5.12-5.24 (1H, m), 5.79 (1H, s), 7.08 (1H, d, J=10.6 Hz), 7.17-7.32 (5H, m), 7.33-7.49 (6H, m), 7.53 (1H, d, J=10.5 Hz), 7.58-7.69 (4H, m);  
25 MASS (ES+): m/e 795.09 (M+1).

Example 41

Compound E41 was obtained from the Compound E40 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=6.9 Hz), 0.91 (3H, t, J=7.3 Hz), 1.21-1.41 (4H, m), 1.38 (3H, d, J=7.0 Hz), 1.51-1.70 (4H, m),  
30 1.70-1.92 (4H, m), 2.08-2.58 (6H, m), 2.96 (1H, dd, J=13.6, 6.4 Hz), 3.16-3.30 (2H, m), 3.56 (1H, d, J=4.6 Hz), 3.82-3.94 (1H, m), 4.13-4.29 (2H, m), 4.67 (1H, brd, J=6.2 Hz), 5.11-5.24 (1H, m), 5.81 (1H, s), 7.11 (1H, d, J=10.3 Hz), 7.16-7.34 (5H, m), 7.50 (1H, d, J=10.4  
35 Hz);  
MASS (ES+): m/e 557.29 (M+1).

Example 42

Compound E42 was obtained from the Compound (105) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.5 Hz), 1.09 (3x3H, s),  
5 1.22 (3H, d, J=7 Hz), 1.28 (3H, s), 1.45 (2H, m), 1.56-1.90 (4H, m),  
2.07-2.40 (6H, m), 2.97 (1H, dd, J=13.5, 6.5 Hz), 3.24 (1H, dd, J=13.5,  
9 Hz), 3.27 (1H, m), 3.87 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7 Hz),  
4.64 (1H, m), 5.19 (1H, ddd, J=10, 9, 6.5 Hz), 5.81 (1H, s), 6.62 (1H,  
brd, J=16 Hz), 6.87 (1H, dt, J=16, 7 Hz), 7.13 (1H, d, J=10 Hz), 7.17-  
10 7.49 (11H, m), 7.53 (1H, d, J=10 Hz), 7.56-7.76 (4H, m);  
MASS (ES-): m/e 777.

Example 43

Compound E43 was obtained from the Compound (105) in a manner similar to Example 2.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.09 (3x3H, s),  
15 1.23 (3H, d, J=7 Hz), 1.28 (3H, s), 1.45 (2H, m), 1.58-1.92 (4H, m),  
2.08-2.40 (6H, m), 2.97 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5,  
9.5 Hz), 3.27 (1H, m), 3.87 (1H, m), 4.21 (1H, dt, J=10, 7.5 Hz), 4.27  
(1H, q, J=7 Hz), 4.67 (1H, dd, J=8, 2.5 Hz), 5.19 (1H, ddd, J=10, 9.5,  
20 6 Hz), 5.81 (1H, s), 6.61 (1H, brd, J=16 Hz), 6.87 (1H, dt, J=16, 7  
Hz), 7.13 (1H, d, J=10.5 Hz), 7.16-7.49 (11H, m), 7.53 (1H, d, J=10  
Hz), 7.56-7.69 (4H, m);  
MASS (ES-): m/e 777.

Example 44

25 Compound E44 was obtained from the Compound (105) in a manner similar to Example 29.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.4 Hz), 0.83 (3H, t, J=7.4  
Hz), 1.10 (3x3H, s), 1.28 (3H, s), 1.44 (2H, m), 1.54-1.90 (6H, m),  
2.08-2.40 (6H, m), 2.97 (1H, dd, J=14, 6 Hz), 3.24 (1H, dd, J=14, 9.5  
30 Hz), 3.27 (1H, m), 3.87 (1H, m), 4.15 (1H, t, J=6 Hz), 4.20 (1H, m),  
4.67 (1H, m), 5.19 (1H, ddd, J=10, 9.5, 6 Hz), 5.78 (1H, s), 6.55 (1H,  
d, J=16 Hz), 6.80 (1H, dt, J=16, 7 Hz), 7.12 (1H, d, J=10.5 Hz), 7.16-  
7.47 (11H, m), 7.53 (1H, d, J=10 Hz), 7.53-7.68 (4H, m);  
MASS (ES-): m/e 791.

35 Example 45

Compound E45 was obtained from the Compound E42 in a manner

similar to Example 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (3x3H, s),  
1.18 (3H, d, J=7 Hz), 1.20-1.33 (4H, m), 1.28 (3H, s), 1.45 (2H, m),  
1.60 (1H, m), 1.71-1.90 (3H, m), 2.08-2.40 (4H, m), 2.51 (2H, m), 2.97  
5 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9 Hz), 3.27 (1H, m),  
3.86 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7 Hz), 4.67 (1H, m), 5.18  
(1H, ddd, J=10, 9, 6 Hz), 5.81 (1H, s), 7.07 (1H, d, J=10.5 Hz), 7.16-  
7.31 (5H, m), 7.33-7.48 (6H, m), 7.57 (1H, d, J=10 Hz), 7.58-7.74 (4H,  
m);  
10 MASS (ES-): m/e 779.

Example 46

Compound E46 was obtained from the Compound E43 in a manner  
similar to Example 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (3x3H, s),  
15 1.16-1.33 (4H, m), 1.18 (3H, d, J=7 Hz), 1.28 (3H, s), 1.46 (2H, m),  
1.58 (1H, m), 1.68-1.88 (3H, m), 2.07-2.40 (4H, m), 2.51 (2H, t, J=7  
Hz), 2.97 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.27  
(1H, m), 3.86 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7 Hz), 4.67 (1H,  
dd, J=8, 2.5 Hz), 5.18 (1H, ddd, J=10, 9.5, 6 Hz), 5.82 (1H, s), 7.08  
20 (1H, d J=10 Hz), 7.16-7.32 (5H, m), 7.33-7.50 (6H, m), 7.58 (1H, d,  
J=10 Hz), 7.58-7.70 (5H, m);  
MASS (ES-): m/e 779.

Example 47

Compound E47 was obtained from the Compound E44 in a manner  
25 similar to Example 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7 Hz), 0.83 (3H, t, J=7 Hz),  
1.11 (9H, s), 1.15-1.26 (4H, m), 1.28 (3H, s), 1.30-1.46 (2H, m),  
1.50-1.85 (6H, m), 2.07-2.48 (6H, m), 2.97 (1H, dd, J=14, 6 Hz), 3.24  
(1H, dd, J=14, 9 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.10-4.23 (2H, m),  
30 4.67 (1H, m), 5.19 (1H, m), 5.80 (1H, s), 7.06 (1H, d, J=10.5 Hz),  
7.16-7.31 (5H, m), 7.32-7.47 (6H, m), 7.54-7.66 (5H, m);  
MASS: (ES+) m/e 795.

Example 48

Compound E48 was obtained from the Compound E44 in a manner  
35 similar to Example 6 except that pyridine hydrofluoride was used  
instead of tetrabutylammonium fluoride.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7 Hz), 0.94 (3H, t, J=7 Hz), 1.20-1.97 (8H, m), 1.29 (3H, s), 2.08-2.40 (6H, m), 2.97 (1H, dd, J=14, 6 Hz), 3.23 (1H, dd, J=14, 9 Hz), 3.26 (1H, m), 3.59 (1H, d, J=5 Hz), 3.87 (1H, m), 4.22 (1H, m), 4.67 (1H, m), 5.19 (1H, ddd, J=10, 9, 6 Hz), 5.84 (1H, s), 6.26 (1H, d, J=16 Hz), 7.00 (1H, dt, J=16, 7 Hz), 7.16 (1H, d, J=10 Hz), 7.19-7.32 (5H, m), 7.50 (1H, d, J=10 Hz);  
MASS: (ES-) m/e 553.

Example 49

Compound E49 was obtained from the Compound E47 in a manner similar to Example 48.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7 Hz), 0.94 (3H, t, J=7 Hz), 1.22-1.40 (4H, m), 1.28 (3H, s), 1.52-1.70 (4H, m), 1.71-1.98 (4H, m), 2.08-2.24 (2H, m), 2.25-2.40 (2H, m), 2.45 (2H, m), 2.96 (1H, ddd, J=13, 6, 5 Hz), 3.18-3.32 (2H, m), 3.50 (1H, d, J=5 Hz), 3.86 (1H, m), 4.14 (1H, m), 4.20 (1H, m), 4.67 (1H, m), 5.19 (1H, ddd, J=10, 9, 6 Hz), 5.82 (1H, s), 7.10 (1H, d, J=10 Hz), 7.16-7.32 (5H, m), 7.54 (1H, d, J=10 Hz);  
MASS (ES+): m/e 557.

Example 50

Compound 50 was obtained from the Compound E42 in a manner similar to Example 48.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.38 (3H, d, J=7 Hz), 1.42-1.93 (6H, m), 2.07-2.40 (6H, m), 2.97 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.65 (1H, d, J=5 Hz), 3.87 (1H, m), 4.22 (1H, dt, J=10.5, 7.5 Hz), 4.44 (1H, dq, J=7, 5 Hz), 4.67 (1H, dd, J=8, 2.5 Hz), 5.19 (1H, ddd, J=10, 9.5, 6 Hz), 5.84 (1H, s), 6.24 (1H, brd, J=16 Hz), 7.01 (1H, dt, J=16, 7 Hz), 7.16 (1H, d, J=10.5 Hz), 7.16-7.32 (5H, m), 7.50 (1H, d, J=10 Hz);  
MASS (ES-): m/e 539.

Example 51

Compound E51 was obtained from the Compound E45 in a manner similar to Example 48.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.20-1.42 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.90 (6H, m), 2.08-2.58 (6H, m), 2.96 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9 Hz), 3.27 (1H, m), 3.57 (1H, d, J=4.5 Hz), 3.86 (1H, m), 4.14-4.29 (2H, m), 4.67 (1H,

dd, J=8, 2.5 Hz), 5.19 (1H, ddd, J=10, 9, 6 Hz), 5.82 (1H, s), 7.10 (1H, d, J=10 Hz), 7.16-7.33 (5H, m), 7.55 (1H, d, J=10 Hz), 3.57 (1H, d, J=4.5 Hz);

MASS (ES-): m/e 541.

5 Example 52

Compound E52 was obtained from the Compound E46 in a manner similar to Example 48.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.5 Hz), 1.20-1.41 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.52-1.90 (6H, m), 2.08-2.58 (6H, m), 2.96 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.27 (1H, m), 3.57 (1H, d, J=5 Hz), 3.86 (1H, m), 4.14-4.29 (2H, m), 4.67 (1H, dd, J=8, 2.5 Hz), 5.18 (1H, ddd, J=10, 9.5, 6 Hz), 5.83 (1H, s), 7.10 (1H, d, J=10 Hz), 7.16-7.31 (5H, m), 7.55 (1H, d, J=10 Hz);

MASS (ES-): m/e 541.

15 Example 53

To a solution of Compound E52 (7.7 mg) in pyridine (0.8 ml) was added (R)-(-)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride (7.7 mg) at 0°C and the mixture was stirred at ambient temperature until the Compound E52 was disappeared. The solvent was evaporated and the residue was purified by preparative thin layer chromatography (hexane/ethyl acetate = 1:3 v/v) to give Compound E53 as an oil (8.4 mg).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.20-1.38 (4H, m), 1.28 (3H, s), 1.44 (3H, d, J=7 Hz), 1.54-1.90 (6H, m), 2.08-2.59 (6H, m), 2.97 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.28 (1H, m), 3.63 (3H, s), 3.88 (1H, m), 4.14-4.25 (2H, m), 4.67 (1H, dd, J=8.5, 3 Hz), 5.19 (1H, ddd, J=10, 9.5, 6 Hz), 5.24 (1H, q, J=7 Hz), 5.81 (1H, s), 7.09 (1H, d, J=10 Hz), 7.16-7.32 (5H, m), 7.40-7.48 (3H, m), 7.56 (1H, d, J=10 Hz), 7.59-7.66 (2H, m);

30 MASS: (ES-) m/e 757.

Example 54

Compound E54 was obtained from the Compound E52 in a manner similar to Example 53 except that (S)-(-)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride was used instead of (R)-(-)-α-methoxy-α-trifluoromethyl-α-phenylacetyl chloride.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.18-1.38 (4H, m),

1, 28 (3H, s), 1, 46-1.87 (6H, m), 1.49 (3H, d, J=7 Hz), 2.09-2.48 (6H, m), 2.96 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.27 (1H, m), 3.58 (3H, s), 3.86 (1H, m), 4.12-4.26 (2H, m), 4.67 (1H, dd, J=8.2 Hz), 5.18 (1H, m), 5.28 (1H, q, J=7 Hz), 5.81 (1H, s), 7.08 (1H, d, J=10.5 Hz), 7.16-7.32 (5H, m), 7.40-7.47 (3H, m), 7.51-7.62 (3H, m);

MASS (ES-): m/e 757.

#### Example 55

Compound E55 was obtained from the Compound 51 in a manner similar to Example 45.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.5 Hz), 1.17-1.34 (4H, m), 1.28 (3H, s), 1.49 (3H, d, J=7 Hz), 1.51-1.63 (3H, m), 1.70-1.88 (3H, m), 2.08-2.50 (6H, m), 2.96 (1H, dd, J=13.5, 6.5 Hz), 3.23 (1H, dd, J=13.5, 9.5 Hz), 3.27 (1H, m), 3.58 (3H, s), 3.86 (1H, m), 4.18 (1H, m), 4.67 (1H, m), 5.18 (1H, m), 5.29 (1H, q, J=7 Hz), 5.80 (1H, s), 7.08 (1H, d, J=10 Hz), 7.16-7.32 (5H, m), 7.40-7.47 (3H, m), 7.51-7.64 (3H, m);

MASS (ES-): m/e 757.

#### Example 56

Compound E56 was obtained from the Compound 51 in a manner similar to Example 46.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.4 Hz), 1.17-1.37 (4H, m), 1.28 (3H, s), 1.44 (3H, d, J=7 Hz), 1.52-1.68 (3H, m), 1.70-1.90 (3H, m), 2.08-2.59 (6H, m), 2.97 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 10 Hz), 3.27 (1H, m), 3.63 (3H, s), 3.86 (1H, m), 4.19 (1H, dt, J=10, 7.5 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.18 (1H, ddd, J=10, 10, 6 Hz), 5.25 (1H, q, J=7 Hz), 5.81 (1H, s), 7.09 (1H, d, J=10 Hz), 7.16-7.32 (5H, m), 7.40-7.48 (3H, m), 7.52-7.66 (2H, m), 7.56 (1H, d, J=10 Hz);

MASS (ES-): m/e 757.

#### Example 57

Compound E57 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.89 (3H, t, J=7.0 Hz), 0.96 (3H, t, J=6.5 Hz), 1.09 (9H, s), 1.17-1.89 (12H, m), 1.23 (3H, d, J=6.9 Hz), 1.99-2.44 (6H, m), 2.98 (1H, dd, J=13.5, 6.5 Hz), 3.20-3.32 (1H, m), 3.23 (1H, dd, J=13.5, 9.5 Hz), 3.80-3.93 (1H, m), 4.12-4.27 (1H, m), 4.27

(1H, q, J=7.0 Hz), 4.67 (1H, brd, J=5.5 Hz), 5.10-5.23 (1H, m), 5.79 (1H, s), 6.61 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 6.7 Hz), 7.12 (1H, d, J=10.3 Hz), 7.16-7.29 (5H, m), 7.29-7.45 (6H, m), 7.48 (1H, d, J=11.0 Hz), 7.55-7.74 (4H, m);

5 MASS (ES+): m/e 821.39 (M+1).

#### Example 58

Compound E58 was obtained from the Compound E57 in a manner similar to Example 16.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.89 (3H, t, J=6.9 Hz), 0.97 (3H, t, J=7.0 Hz), 1.11 (9H, s), 1.16-1.67 (12H, m), 1.19 (3H, d, J=7.0 Hz), 1.68-1.88 (4H, m), 2.00-2.45 (4H, m); 2.51 (2H, brt, J=6.9 Hz), 2.98 (1H, dd, J=13.1, 6.3 Hz), 3.21-3.32 (1H, m), 3.23 (1H, dd, J=13.1, 9.2 Hz), 3.81-3.92 (1H, m), 4.13 (1H, q, J=7.1 Hz), 4.15-4.23 (1H, m), 4.68 (1H, brd, J=5.7 Hz), 5.10-5.22 (1H, m), 5.80 (1H, s), 7.07 (1H, d, J=10.3 Hz), 7.16-7.31 (6H, m), 7.33-7.48 (5H, m), 7.52 (1H, d, J=10.2 Hz), 7.58-7.75 (4H, m);

15 MASS (ES+): m/e 823.31 (M+1).

#### Example 59

Compound E59 was obtained from the Compound E57 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.89 (3H, t, J=6.5 Hz), 0.96 (3H, t, J=6.9 Hz), 1.12-1.41 (7H, m), 1.38 (3H, d, J=7.4 Hz), 1.41-1.69 (5H, m), 1.70-1.88 (4H, m), 2.00-2.58 (6H, m), 2.98 (1H, dd, J=12.5, 6.2 Hz), 3.19-3.31 (1H, m), 4.12-4.29 (1H, dd, J=12.5, 9.0 Hz), 3.55 (1H, d, J=4.8 Hz), 3.80-3.93 (1H, m), 4.12-4.29 (2H, m), 4.67 (1H, brd, J=5.4 Hz), 5.10-5.22 (1H, m), 5.81 (1H, s), 7.10 (1H, d, J=9.9 Hz), 7.16-7.32 (5H, m), 7.49 (1H, d, J=10.5 Hz);

25 MASS (ES+): m/e 585.34 (M+1).

#### Example 60

30 Compound E60 was obtained in a manner similar to Example 3.

#### Example 61

A solution of the Compound E60 (88 mg) in methanol (3 ml) was hydrogenated in the presence of palladium hydroxide, 20 wt% Pd (dry basis) on carbon (Pearlman's catalyst) (30 mg) for 2 hours. The catalyst was filtered off and the filtrate was concentrated in vacuo. The residue was purified by preparative thin layer chromatography

(eluting with chloroform : methanol = 20:1 v/v) to give Compound E61 as an amorphous (76 mg).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.04 (3x3H, s), 1.22-1.43 (4H, m), 1.38 (3H, d, J=7 Hz), 1.56-1.93 (6H, m), 2.17 (1H, m), 2.26-2.58 (3H, m), 2.91 (1H, dd, J=13, 5 Hz), 3.02 (1H, m), 3.19 (1H, dd, J=13, 11 Hz), 3.57 (1H, d, J=5 Hz), 3.91 (1H, m), 4.13 (1H, d, J=10.5 Hz), 4.24 (1H, dq, J=7, 5 Hz), 4.33 (1H, dt, J=10, 7.5 Hz), 4.60 (1H, m), 5.02 (1H, ddd, J=11, 10, 5 Hz), 6.23 (1H, d, J=10.5 Hz), 6.25 (1H, d, J=10 Hz), 7.12-7.32 (6H, m);

10 MASS: (ES<sup>+</sup>): m/e 557.

#### Example 62

Compound E62 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.71 (3H, d, J=6.9 Hz), 0.87 (3H, d, J=6.6 Hz), 1.09 (9H, s), 1.15 (3H, s), 1.36-1.92 (10H, m), 2.13-2.37 (3H, m), 2.99 (1H, dd, J=13.9, 7.0 Hz), 3.21 (1H, dd, J=13.9, 8.8 Hz), 3.26-3.36 (2H, m), 3.83-3.93 (1H, m), 4.17-4.31 (2H, m), 4.66-4.72 (1H, m), 5.21 (1H, ddd, J=10.6, 8.8, 7.0 Hz), 5.78 (1H, s), 6.61 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 6.6 Hz), 7.13 (1H, d, J=10.6 Hz), 7.16-7.50 (10H, m), 7.54-7.74 (6H, m);

20 MASS: (ES<sup>+</sup>): m/e 793.32 (M+1).

#### Example 63

Compound E63 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70 (3H, d, J=7.0 Hz), 0.87 (3H, d, J=6.6 Hz), 1.10 (9H, s), 1.15 (3H, s), 1.18 (3H, d, J=6.6 Hz), 1.21-1.88 (11H, m), 2.14-2.37 (2H, m), 2.51 (2H, dt, J=7.3, 2.2 Hz), 2.99 (1H, dd, J=13.9, 7.0 Hz), 3.20 (1H, dd, J=13.9, 8.8 Hz), 3.26-3.37 (1H, m), 3.82-3.92 (1H, m), 4.13-4.27 (2H, m), 4.66-4.71 (1H, m), 5.20 (1H, ddd, J=10.3, 8.8, 7.0 Hz), 5.77 (1H, s), 7.07 (1H, d, J=10.3 Hz), 7.16-7.31 (5H, m), 7.33-7.48 (5H, m), 7.58-7.74 (6H, m);

30 MASS: (ES<sup>+</sup>): m/e 795.29 (M+1).

#### Example 64

Compound E64 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.71 (3H, d, J=7.0 Hz), 0.88 (3H, d, J=6.6 Hz), 1.15 (3H, s), 1.21-1.43 (4H, m), 1.38 (3H, d, J=7.0 Hz), 1.52-1.72 (3H, m), 1.72-1.91 (3H, m), 2.11-2.57 (4H, m), 2.99 (1H, dd, J=13.6, 7.0 Hz), 3.20 (1H, dd, J=13.6, 8.8 Hz), 3.26-3.38 (2H, m),

35

3.57 (1H, brs), 3.83-3.93 (1H, m), 4.16-4.28 (2H, m), 4.66-4.73 (1H, m), 5.15-5.26 (1H, m), 5.85 (1H, s), 7.12 (1H, d, J=10.3 Hz), 7.16-7.32 (5H, m), 7.61 (1H, d, J=10.3 Hz);

MASS: (ES+): m/e 557.39 (M+1).

5 Example 65

Compound E65 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.08 (9H, s), 1.21 (3H, d, J=7.0 Hz), 1.32-1.84 (7H, m), 2.10-2.39 (3H, m), 2.85 (1H, dd, J=13.6, 10.6 Hz), 3.00 (1H, dd, J=14.3, 7.0 Hz), 3.04-3.15 (1H, m), 3.18 (1H, dd, J=13.6, 10.6 Hz), 3.39 (1H, dd, J=14.3, 8.4 Hz), 3.91-4.01 (1H, m), 4.21-4.32 (1H, m), 4.26 (1H, q, J=7.0 Hz), 4.59-4.64 (1H, m), 4.81-4.91 (1H, m), 5.06 (1H, dt, J=10.6, 5.1 Hz), 6.32 (1H, d, J=9.9 Hz), 6.45 (1H, d, J=10.6 Hz), 6.57 (1H, d, J=15.8 Hz), 6.82 (1H, dt, J=15.8, 7.0 Hz), 7.13-7.27 (5H, m), 7.29-7.50 (10H, m), 7.55-7.68 (5H, m), 7.74-7.83 (3H, m);

MASS: (ES-): m/e 875.40 (M-1).

Example 66

Compound E66 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.13-1.26 (4H, m), 1.18 (3H, d, J=7.0 Hz), 1.34-1.46 (2H, m), 1.54-1.81 (4H, m), 2.15-2.41 (2H, m), 2.46 (2H, dt, J=7.3, 1.8 Hz), 2.85 (1H, dd, J=13.2, 5.1 Hz), 3.00 (1H, dd, J=13.9, 7.3 Hz), 3.04-3.15 (1H, m), 3.18 (1H, dd, J=13.2, 10.6 Hz), 3.39 (1H, dd, J=13.9, 8.4 Hz), 3.90-4.00 (1H, m), 4.17 (1H, q, J=7.0 Hz), 4.18-4.29 (1H, m), 4.58-4.64 (1H, m), 4.81-4.91 (1H, m), 5.06 (1H, dt, J=10.6, 5.1 Hz), 6.30 (1H, d, J=9.9 Hz), 6.46 (1H, d, J=10.6 Hz), 7.09-7.27 (5H, m), 7.31-7.48 (10H, m), 7.58-7.68 (5H, m), 7.74-7.82 (3H, m);

MASS: (ES+): m/e 879.31 (M+1).

Example 67

30 Compound E67 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.16-1.40 (4H, m), 1.36 (3H, d, J=7.0 Hz), 1.47-1.87 (6H, m), 2.14-2.51 (4H, m), 2.86 (1H, dd, J=13.6, 5.5 Hz), 3.02 (1H, dd, J=14.3, 7.3 Hz), 3.06-3.14 (1H, m), 3.19 (1H, dd, J=13.6, 10.6 Hz), 3.39 (1H, dd, J=14.3, 8.4 Hz), 3.56 (1H, br), 3.91-4.01 (1H, m), 4.16-4.31 (2H, m), 4.59-4.66 (1H, m), 4.81-4.92 (1H, m), 5.08 (1H, dt, J=10.6, 5.5 Hz), 6.32 (1H, d, J=9.9 Hz), 6.47 (1H, d, J=10.6 Hz),

7.11-7.30 (6H, m), 7.35 (1H, dd, J=8.4, 1.5 Hz), 7.41-7.51 (2H, m),  
7.67 (1H, s), 7.74-7.84 (3H, m);

MASS: (ES+): m/e 641.32 (M+1).

Example 68

5 Compound E68 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.08 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.30-  
1.85 (7H, m), 2.11-2.26 (2H, m), 2.29-2.38 (1H, m), 2.86 (1H, d,  
J=16.5 Hz), 2.94 (1H, dd, J=13.2, 5.3 Hz), 3.11-3.22 (1H, m), 3.31 (1H,  
dd, J=13.2, 10.3 Hz), 3.62 (1H, d, J=16.5 Hz), 3.90-4.02 (3H, m),  
10 4.16-4.27 (1H, m), 4.27 (1H, q, J=7 Hz), 4.64-4.70 (1H, m), 5.15 (1H,  
dt, J=10.3, 5.3 Hz), 6.32 (1H, s), 6.58 (1H, d, J=15.8 Hz), 6.84 (1H,  
dt, J=15.8, 6.8 Hz), 7.15-7.29 (10H, m), 7.29-7.46 (6H, m), 7.50 (1H,  
d, J=10.3 Hz), 7.55-7.75 (4H, m);

MASS: (ES+): m/e 839.28 (M+1).

15 Example 69

Compound E69 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.18 (3H, d, J=7.0 Hz), 1.15-  
1.35 (2H, m), 1.36-1.49 (1H, m), 1.54-1.84 (7H, m), 2.10-2.41 (2H, m),  
2.49 (2H, dt, J=7.7, 2.6 Hz), 2.85 (1H, d, J=15.8 Hz), 2.93 (1H, dd,  
20 J=13.2, 5.1 Hz), 3.11-3.22 (1H, m), 3.30 (1H, dd, J=13.2, 10.3 Hz),  
3.62 (1H, d, J=16.5 Hz), 3.89-3.99 (1H, m), 3.97 (1H, d, J=16.5 Hz),  
3.98 (1H, d, J=15.8 Hz), 4.13-4.24 (1H, m), 4.15 (1H, q, J=7.0 Hz),  
4.64-4.70 (1H, m), 5.14 (1H, dt, J=10.3, 5.1 Hz), 6.32 (1H, s), 7.12-  
7.31 (10H, m), 7.32-7.47 (6H, m), 7.53 (1H, d, J=10.3 Hz), 7.58-7.68  
25 (4H, m);

MASS: (ES+): m/e 841.22 (M+1).

Example 70

Compound E70 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.37 (3H, d, J=7.0 Hz), 1.51-1.86 (9H, m),  
30 2.06-2.26 (2H, m), 2.27-2.54 (3H, m), 2.86 (1H, d, J=16.2 Hz), 2.92  
(1H, dd, J=13.2, 5.1 Hz), 3.09-3.21 (1H, m), 3.29 (1H, dd, J=13.2,  
10.3 Hz), 3.55 (1H, d, J=4.5 Hz), 3.60 (1H, d, J=16.2 Hz), 3.88-4.02  
(1H, m), 3.97 (2H, d, J=16.2 Hz), 4.13-4.27 (2H, m), 4.63-4.70 (1H, m),  
5.14 (1H, dt, J=10.3, 5.1 Hz), 6.39 (1H, s), 7.13-7.31 (10H, m), 7.51  
35 (1H, d, J=10.3 Hz);

MASS: (ES+): m/e 603.35 (M+1).

Example 71

Compound E71 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.0 Hz), 1.10 (9H, s), 1.23 (3H, d, J=7.0 Hz), 1.29 (3H, s), 1.39-1.91 (8H, m), 2.08-2.38 (4H, m),  
5 3.13 (1H, dd, J=13.2, 6.2 Hz), 3.20-3.29 (1H, m), 3.42 (1H, dd, J=13.2, 9.9 Hz), 3.84-3.93 (1H, m), 4.17-4.27 (1H, m), 4.28 (1H, q, J=7.0 Hz), 4.62-4.68 (1H, m), 5.30 (1H, dt, J=9.9, 6.2 Hz), 5.87 (1H, s), 6.62 (1H, d, J=15.4 Hz), 6.88 (1H, dt, J=15.4, 6.6 Hz), 7.15 (1H, d, J=9.9 Hz), 7.31-7.49 (9H, m), 7.57-7.74 (6H, m), 7.74-7.83 (3H, m);  
10 MASS: (ES<sup>+</sup>): m/e 829.43 (M+1).

Example 72

Compound E72 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.00-1.34 (4H, m), 1.10 (9H, s), 1.19 (3H, d, J=6.6 Hz), 1.28 (3H, s), 1.35-1.89 (12H, m),  
15 2.07-2.40 (4H, m), 2.51 (2H, dt, J=7.3, 2.2 Hz), 3.12 (1H, dd, J=13.6, 5.9 Hz), 3.18-3.30 (1H, m), 3.41 (1H, dd, J=13.6, 9.9 Hz), 3.81-3.92 (1H, m), 4.12-4.27 (3H, m), 4.61-4.67 (1H, m), 5.29 (1H, dt, J=9.9, 5.9 Hz), 5.83 (1H, s), 7.08 (1H, d, J=10.3 Hz), 7.32-7.49 (9H, m), 7.57-7.73 (6H, m), 7.73-7.83 (3H, m);  
20 MASS: (ES<sup>+</sup>): m/e 831.35 (M+1).

Example 73

Compound E73 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.20-1.40 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.52-1.90 (6H, m), 2.07-2.57 (6H, m),  
25 3.12 (1H, dd, J=13.6, 5.9 Hz), 3.19-3.29 (1H, m), 3.41 (1H, dd, J=13.6, 9.9 Hz), 3.56 (1H, d, J=4.8 Hz), 3.82-3.92 (1H, m), 4.15-4.29 (2H, m), 4.62-4.68 (1H, m), 5.30 (1H, dt, J=9.9, 5.9 Hz), 5.88 (1H, s), 7.11 (1H, d, J=10.3 Hz), 7.35-7.40 (1H, m), 7.40-7.49 (2H, m), 7.62 (1H, d, J=10.3 Hz), 7.69 (1H, s), 7.74-7.83 (3H, m);  
30 MASS: (ES<sup>+</sup>): m/e 593.35 (M+1).

Example 74

Compound E74 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.15-1.88 (5H, m), 1.19-1.29 (3H, m), 2.14-2.37 (4H, m), 2.86 (1H, dd, J=13.2, 5.1 Hz), 2.98 (1H, dd, J=14.7, 5.9 Hz), 3.05-3.16 (1H, m), 3.18 (1H, dd, J=13.2, 10.6 Hz),  
35 3.35 (1H, dd, J=14.7, 8.8 Hz), 3.77 (3H, s), 3.93-4.02 (1H, m), 4.21-

4.33 (3H, m), 4.59-4.64 (1H, m), 4.81 (1H, dt, J=9.5, 6.6 Hz), 5.08 (1H, dt, J=10.6, 5.1 Hz), 6.36 (1H, d, J=9.9 Hz), 6.45 (1H, d, J=10.6 Hz), 6.58 (1H, d, J=15.4 Hz), 6.84 (1H, dt, J=15.4, 7.0 Hz), 6.87 (1H, s), 7.08-7.26 (7H, m), 7.32-7.49 (7H, m), 7.56-7.68 (6H, m);

5 MASS (ES-) m/e 878.36 (M-1).

#### Example 75

Compound E75 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.13-1.32 (3H, m), 1.38-1.50 (2H, m), 1.54-1.84 (5H, m), 2.16-2.38 (4H, m), 2.45-2.53 (2H, m), 2.86 (1H, dd, J=13.2, 5.1 Hz), 2.99 (1H, dd, J=14.7, 5.9 Hz), 3.05-3.16 (1H, m), 3.18 (1H, dd, J=13.2, 10.6 Hz), 3.35 (1H, dd, J=14.7, 9.5 Hz), 3.77 (3H, s), 3.92-4.01 (1H, m), 4.14-4.24 (1H, m), 4.26 (2H, q, J=7.0 Hz), 4.59-4.64 (1H, m), 4.82 (1H, dt, J=9.5, 5.9 Hz), 5.08 (1H, dt, J=10.6, 5.1 Hz), 6.34 (1H, d, J=9.9 Hz), 6.47 (1H, d, J=10.6 Hz), 6.87 (1H, s), 7.09-7.31 (7H, m), 7.33-7.49 (7H, m), 7.58-7.67 (6H, m);

15 MASS (ES+): m/e 882.37 (M+1).

#### Example 76

Compound E76 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.19-1.40 (4H, m), 1.38 (3H, d, J=7.0 Hz), 1.50-1.86 (6H, m), 2.13-2.55 (4H, m), 2.85 (1H, dd, J=13.6, 5.1 Hz), 2.98 (1H, dd, J=14.7, 6.6 Hz), 3.04-3.15 (1H, m), 3.17 (1H, dd, J=13.6, 10.6 Hz), 3.34 (1H, dd, J=14.7, 8.8 Hz), 3.52-3.59 (1H, m), 3.73 (3H, s), 3.92-4.01 (1H, m), 4.17-4.31 (2H, m), 4.58-4.65 (1H, m), 4.81 (1H, ddd, J=9.5, 8.8, 6.6 Hz), 5.08 (1H, dt, J=10.6, 5.1 Hz), 6.34 (1H, d, J=9.5 Hz), 6.46 (1H, d, J=10.6 Hz), 6.87 (1H, s), 7.08-7.31 (9H, m), 7.60 (1H, d, J=8.1 Hz);

25 MASS (ES+): m/e 644.48 (M+1).

#### Example 77

Compound E77 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.38-1.91 (7H, m), 2.08-2.39 (5H, m), 2.30 (3H, s), 2.91 (1H, dd, J=13.6, 6.2 Hz), 3.20 (1H, dd, J=13.6, 10.3 Hz), 3.23-3.33 (1H, m), 3.82-3.92 (1H, m), 4.16-4.25 (1H, m), 4.27 (1H, q, J=6.6 Hz), 4.64-4.70 (1H, m), 5.16 (1H, dt, J=10.3, 6.2 Hz), 5.84 (1H, s), 6.61 (1H, d, J=15.7 Hz), 6.87 (1H, dt, J=15.7, 6.6 Hz), 7.05-7.13 (4H, m), 7.14 (1H, d, J=9.5 Hz), 7.31-7.45 (6H, m),

30  
35

7.51 (1H, d, J=10.3 Hz), 7.56-7.68 (4H, m);

MASS (ES+): m/e 793.57 (M+1).

Example 78

Compound E78 was obtained in a manner similar to Example 4.

5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.7 Hz), 1.10 (9H, s), 1.18 (3H, d, J=6.6 Hz), 1.28 (3H, s), 1.38-1.88 (9H, m), 2.07-2.40 (5H, m), 2.30 (3H, s), 2.51 (2H, dt, J=7.3, 2.6 Hz), 2.91 (1H, dd, J=13.2, 6.2 Hz), 3.20 (1H, dd, J=13.2, 9.9 Hz), 3.24-3.33 (1H, m), 3.81-3.91 (1H, m), 4.14-4.24 (1H, m), 4.18 (1H, q, J=6.6 Hz), 4.64-4.70 (1H, m), 5.16  
10 (1H, dt, J=9.9, 6.2 Hz), 5.84 (1H, s), 7.05-7.15 (5H, m), 7.33-7.48 (6H, m), 7.55 (1H, d, J=9.9 Hz), 7.59-7.67 (4H, m);

MASS (ES+): m/e 795.52 (M+1).

Example 79

Compound E79 was obtained in a manner similar to Example 6.

15 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.20-1.41 (6H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.52-1.89 (4H, m), 2.07-2.40 (4H, m), 2.30 (3H, s), 2.46 (2H, dt, J=12.1, 7.3 Hz), 2.91 (1H, dd, J=13.7, 6.2 Hz), 3.20 (1H, dd, J=13.7, 9.9 Hz), 3.25-3.32 (1H, m), 3.55 (1H, d, J=4.8 Hz), 3.81-3.91 (1H, m), 4.14-4.28 (2H, m), 4.64-4.70 (1H, m),  
20 5.16 (1H, dt, J=9.9, 6.2 Hz), 5.85 (1H, s), 7.05-7.15 (5H, m), 7.53 (1H, d, J=9.9 Hz);

MASS (ES+): m/e 557.41 (M+1).

Example 80

Compound E80 was obtained in a manner similar to Example 1.

25 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.2 Hz), 1.09 (9H, s), 1.22 (3H, d, J=6.9 Hz), 1.29 (3H, s), 1.38-1.51 (1H, m), 1.56-1.71 (1H, m), 1.73-2.43 (H, m), 3.13 (1H, dd, J=15.0, 5.7 Hz), 3.52 (1H, dd, J=15.0, 9.9 Hz), 3.73-3.84 (1H, m), 3.87-3.98 (1H, m), 4.17-4.26 (1H, m), 4.27 (1H, q, J=6.9 Hz), 4.68 (1H, dd, J=7.5, 2.4 Hz), 5.57 (1H, dt, J=9.9, 5.7 Hz), 5.87 (1H, s), 6.60 (1H, d, J=15.6 Hz), 6.86 (1H, dt, J=15.6, 6.3 Hz), 7.08-7.14 (1H, m), 7.15-7.21 (2H, m), 7.30-7.52 (6H, m),  
30 7.55-7.68 (6H, m), 8.43-8.48 (1H, m);

MASS (ES+): m/e 780.56 (M+1).

Example 81

35 Compound E81 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.2 Hz), 1.10 (9H, s), 1.18

(3H, d, J=6.6 Hz), 1.20-2.46 (14H, m), 1.26 (3H, s), 2.46-2.57 (2H, m), 3.18-3.32 (1H, m), 3.58-3.97 (3H, m), 4.14-4.26 (2H, m), 4.66-4.73 (1H, m), 5.53-5.63 (1H, m), 5.90 (1H, s), 7.04-7.14 (1H, m), 7.28-7.48 (8H, m), 7.54-7.86 (6H, m), 8.50-8.58 (1H, m);

5 MASS (ES+): m/e 782.57 (M+1).

Example 82

Compound E82 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.2 Hz), 1.17-1.96 (12H, m), 1.29 (3H, s), 1.38 (3H, d, J=6.9 Hz), 2.06-2.57 (4H, m), 3.11-3.24 (1H, m), 3.12 (1H, dd, J=15.0, 5.7 Hz), 3.52 (1H, dd, J=15.0, 10.2 Hz), 3.74-3.84 (1H, m), 3.88-3.98 (1H, m), 4.14-4.28 (2H, m), 4.68 (1H, dd, J=7.5, 2.4 Hz), 5.58 (1H, dt, J=10.2, 5.7 Hz), 5.92 (1H, s), 7.07-7.12 (1H, m), 7.14-7.20 (2H, m), 7.42-7.52 (1H, m), 7.57 (1H, dt, J=7.5, 1.8 Hz), 8.42-8.47 (1H, s);

15 MASS (ES+): m/e 544.49 (M+1).

Example 83

Compound E83 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.5 Hz), 1.09 (9H, s), 1.14 (3H, d, J=7.3 Hz), 1.29 (3H, s), 1.34-1.91 (6H, m), 2.00-2.40 (6H, m), 2.16 (3H, s), 2.92 (1H, dd, J=13.7, 6.0 Hz), 3.14-3.34 (2H, m), 3.78-3.94 (1H, m), 4.16-4.33 (2H, m), 4.67 (1H, brd, J=6.0 Hz), 5.08-5.24 (1H, m), 5.90 (1H, brs), 6.61 (1H, brd, J=15.8 Hz), 6.80-6.94 (1H, m), 7.05-7.24 (4H, m), 7.30-7.48 (7H, m), 7.50-7.71 (6H, m);

MASS (ES+): m/e 836.37 (M+1).

25 Example 84

Compound E84 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.13-1.88 (10H, m), 1.21 (3H, d, J=6.8 Hz), 1.28 (3H, s), 2.07-2.22 (2H, m), 2.16 (3H, s), 2.24-2.39 (2H, m), 2.44-2.56 (2H, m), 2.84-2.97 (1H, m), 3.12-3.34 (2H, m), 3.77-3.94 (1H, m), 4.10-4.34 (2H, m), 4.66 (1H, brd, J=6.6 Hz), 5.07-5.21 (1H, m), 5.88 (1H, brs), 7.06 (1H, d, J=10.6 Hz), 7.13 (1H, s), 7.18 (2H, d, J=8.1 Hz), 7.31-7.50 (7H, m), 7.53-7.71 (6H, m);

MASS (ES+): m/e 838.48 (M+1).

35 Example 85

Compound E85 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 1.21-1.91 (10H, m), 1.29 (3H, s), 1.39 (3H, d, J=7.3 Hz), 2.08-2.24 (2H, m), 2.17 (3H, s), 2.26-2.40 (2H, m), 2.41-2.58 (2H, m), 2.91 (1H, dd, J=13.6, 5.5 Hz), 3.14-3.34 (2H, m), 3.51-3.61 (1H, m), 3.75-3.92 (1H, m), 4.13-4.30 (2H, m), 4.67 (1H, brd, J=6.2 Hz), 5.08-5.22 (1H, m), 5.90 (1H, s), 7.10 (1H, d, J=9.9 Hz), 7.16 (1H, s), 7.19 (2H, d, J=8.6 Hz), 7.40 (2H, d, J=8.6 Hz), 7.56 (1H, d, J=9.2 Hz);

MASS (ES<sup>+</sup>): m/e 600.42 (M+1).

#### Example 86

10 Compound E86 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.3 Hz), 1.09 (9H, s), 1.19-2.35 (14H, m), 1.22 (3H, d, J=6.6 Hz), 1.27 (3H, s), 2.93 (1H, dt, J=13.2, 2.9 Hz), 3.04 (1H, dd, J=13.9, 7.7 Hz), 3.21 (1H, dd, J=13.9, 7.9 Hz), 4.00 (1H, brd, J=12.5 Hz), 4.17-4.28 (1H, m), 4.27 (1H, q, J=6.6 Hz), 4.98-5.08 (1H, m), 5.36 (1H, dt, J=10.6, 7.9 Hz), 5.95 (1H, s), 6.49 (1H, d, J=10.3 Hz), 6.62 (1H, d, J=15.8 Hz), 6.85 (1H, dt, J=15.8, 7.0 Hz), 7.15-7.48 (11H, m), 7.51 (1H, d, J=10.6 Hz), 7.55-7.70 (4H, m);

MASS (ES<sup>+</sup>): m/e 793.52 (M+1).

#### 20 Example 87

Compound E87 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.3 Hz), 1.03-1.65 (9H, m), 1.10 (9H, s), 1.18 (3H, d, J=7.0 Hz), 1.27 (3H, s), 1.68-1.84 (2H, m), 1.91-2.34 (5H, m), 2.51 (2H, dt, J=7.2, 1.8 Hz), 2.94 (1H, dt, J=13.6, 2.9 Hz), 3.04 (1H, dd, J=13.9, 7.1 Hz), 3.21 (1H, dd, J=13.9, 7.7 Hz), 3.99 (1H, brd, J=12.8 Hz), 4.13-4.26 (2H, m), 4.98-5.07 (1H, m), 5.36 (1H, dt, J=10.3, 7.5 Hz), 5.93 (1H, s), 6.45 (1H, d, J=10.3 Hz), 7.15-7.31 (5H, m), 7.32-7.49 (6H, m), 7.54 (1H, d, J=10.3 Hz), 7.58-7.71 (4H, m);

30 MASS (ES<sup>+</sup>): m/e 795.53 (M+1).

#### Example 88

Compound E88 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.3 Hz), 1.17-1.43 (4H, m), 1.27 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.45-1.69 (6H, m), 1.70-1.86 (1H, m), 1.90-2.17 (4H, m), 2.19-2.34 (1H, m), 2.35-2.58 (2H, m), 2.93 (1H, dt, J=13.2, 2.6 Hz), 3.03 (1H, dd, J=13.9, 7.3 Hz), 3.21 (1H, dd,

J=13.9, 7.7 Hz), 3.58 (1H, d, J=4.8 Hz), 3.99 (1H, brd, J=12.8 Hz), 4.15-4.30 (2H, m), 5.00-5.06 (1H, m), 5.36 (1H, dt, J=10.3, 7.5 Hz), 6.02 (1H, s), 6.50 (1H, d, J=10.3 Hz), 7.15-7.33 (5H, m), 7.53 (1H, d, J=10.3 Hz);

5 MASS (ES+): m/e 557.39 (M+1).

Example 89

Compound E89 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.77 (3H, t, J=7.3 Hz), 1.18-2.38 (14H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.3 Hz), 2.92 (1H, dt, J=13.2, 2.6 Hz),  
10 3.04 (1H, dd, J=13.9, 7.3 Hz), 3.21 (1H, dd, J=13.9, 7.7 Hz), 3.66 (1H, d, J=5.1 Hz), 3.95-4.06 (1H, m), 4.17-4.31 (1H, m), 4.39-4.51 (1H, m), 5.03 (1H, brd, J=5.5 Hz), 5.36 (1H, dt, J=10.3, 7.7 Hz), 5.99 (1H, s), 6.24 (1H, d, J=15.8 Hz), 6.53 (1H, d, J=10.3 Hz), 7.00 (1H, dt, J=15.8, 7.0 Hz), 7.15-7.35 (5H, m), 7.48 (1H, d, J=10.3 Hz);

15 MASS (ES+): m/e 555.40 (M+1).

Example 90

Compound E90 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.21 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.38-2.42 (12H, m), 2.90-2.99 (1H, m),  
20 2.99 (3H, s), 3.20 (1H, dd, J=13.6, 8.8 Hz), 3.26-3.36 (1H, m), 3.79-3.92 (1H, m), 4.17-4.32 (2H, m), 4.68 (1H, brd, J=8.1 Hz), 5.10-5.21 (1H, m), 5.85 (1H, s), 6.42 (1H, s), 6.62 (1H, brd, J=15.6 Hz), 6.87 (1H, dt, J=15.6, 6.6 Hz), 7.07 (1H, d, J=10.3 Hz), 7.13 (2H, d, J=8.4 Hz), 7.23 (2H, d, J=8.4 Hz), 7.31-7.69 (10H, m);

25 MASS (ES-) m/e 870.56 (M-1).

Example 91

Compound E91 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.21 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.37-1.66 (7H, m), 1.71-1.91 (3H, m),  
30 2.07-2.39 (4H, m), 2.51 (2H, dt, J=7.0, 2.2 Hz), 2.95 (1H, dd, J=13.6, 6.6 Hz), 2.99 (3H, s), 3.20 (1H, dd, J=13.6, 9.2 Hz), 3.26-3.36 (1H, m), 3.79-3.91 (1H, m), 4.14-4.24 (1H, m), 4.25 (1H, q, J=7.0 Hz), 4.69 (1H, brd, J=7.0 Hz), 5.09-5.21 (1H, m), 5.90 (1H, s), 6.46 (1H, s), 7.03 (1H, d, J=9.9 Hz), 7.12 (2H, d, J=8.4 Hz), 7.23 (2H, d, J=8.4 Hz),  
35 7.32-7.50 (6H, m), 7.57-7.70 (5H, m);

MASS (ES-) m/e 872.46 (M-1).

Example 92

Compound E92 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.21-1.41 (4H, m),  
1.29 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.51-1.69 (3H, m), 1.70-1.90 (3H,  
5 m), 2.08-2.58 (6H, m), 2.95 (1H, dd, J=13.9, 7.0 Hz), 2.99 (3H, s),  
3.20 (1H, dd, J=13.9, 9.5 Hz), 3.26-3.37 (1H, m), 3.55 (1H, brd, J=4.0  
Hz), 3.79-3.91 (1H, m), 4.15-4.29 (2H, m), 4.69 (1H, brd, J=7.3 Hz),  
5.15 (1H, dt, J=9.6, 6.6 Hz), 5.94 (1H, s), 6.56 (1H, s), 7.06 (1H, d,  
J=10.3 Hz), 7.13 (2H, d, J=8.4 Hz), 7.22 (2H, d, J=8.4 Hz), 7.60 (2H,  
10 d, J=10.3 Hz);

MASS (ES<sup>+</sup>): m/e 636.51 (M+1):

Example 93

Compound E93 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.23  
15 (3H, d, J=6.6 Hz), 1.30 (3H, s), 1.36-1.93 (6H, m), 2.08-2.41 (6H, m),  
3.02 (1H, dd, J=13.5, 6.2 Hz), 3.22-3.38 (2H, m), 3.82-3.96 (1H, m),  
4.15-4.28 (1H, m), 4.27 (1H, q, J=6.6 Hz), 4.69 (1H, brd, J=6.0 Hz),  
5.17-5.30 (1H, m), 5.85 (1H, s), 6.62 (1H, d, J=15.3 Hz), 6.87 (1H, dt,  
J=15.3, 7.0 Hz), 7.13 (1H, d, J=10.3 Hz), 7.27-7.48 (11H, m), 7.49-  
20 7.69 (9H, m);

MASS (ES<sup>+</sup>): m/e 855.61 (M+1).

Example 94

Compound E94 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.4 Hz), 1.10 (9H, s), 1.19  
25 (3H, d, J=6.9 Hz), 1.20-1.34 (7H, m), 1.29 (3H, s), 1.39-1.60 (3H, m),  
1.69-1.90 (3H, m), 2.08-2.40 (4H, m), 2.52 (2H, dt, J=7.3, 2.2 Hz),  
3.02 (1H, dd, J=13.5, 6.3 Hz), 3.20-3.38 (2H, m), 3.82-3.94 (1H, m),  
4.12-4.26 (2H, m), 4.69 (1H, brd, J=5.7 Hz), 5.15-5.29 (1H, m), 5.84  
(1H, s), 7.07 (1H, d, J=10.3 Hz), 7.27-7.47 (12H, m), 7.48-7.69 (8H,  
30 m);

MASS (ES<sup>+</sup>): m/e 857.66 (M+1).

Example 95

Compound E95 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 1.21-1.41 (4H, m),  
35 1.27 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.53-1.70 (3H, m), 1.71-1.90 (3H,  
m), 2.08-2.58 (6H, m), 3.01 (1H, dd, J=13.9, 6.1 Hz), 3.21-3.38 (2H,

m), 3.56 (1H, d, J=4.7 Hz), 3.82-3.94 (1H, m), 4.14-4.30 (2H, m), 4.69 (1H, brd, J=5.7 Hz), 5.16-5.29 (1H, m), 5.87 (1H, s), 7.11 (1H, d, J=10.0 Hz), 7.23-7.36 (3H, m), 7.38-7.46 (2H, m), 7.47-7.64 (5H, m); MASS (ES+): m/e 619.55 (M+1).

5 Example 96

Compound E96 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=7 Hz), 1.29 (3H, s), 1.45 (2H, m), 1.58-1.91 (4H, m), 2.07-2.40 (6H, m), 2.90 (1H, dd, J=13.5, 6 Hz), 3.19 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (2x3H, s), 3.86 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7 Hz), 4.67 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.90 (1H, s), 6.62 (1H, d, J=15.5 Hz), 6.74-6.80 (3H, m), 6.86 (1H, dt, J=15.5, 7 Hz), 7.14 (1H, d, J=10 Hz), 7.30-7.48 (6H, m), 7.54 (1H, d, J=10 Hz), 7.57-7.68 (5H, m);  
15 MASS (ES+): m/e 839.

Example 97

Compound E97 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=6.5 Hz), 1.18-1.32 (4H, m), 1.29 (3H, s), 1.45 (2H, m), 20 1.58-1.69 (1H, m), 1.70-1.89 (3H, m), 2.08-2.40 (4H, m), 2.51 (2H, m), 2.90 (1H, dd, J=13.5, 6 Hz), 3.20 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (2x3H, s), 3.85 (1H, m), 4.14-4.25 (2H, m), 4.67 (1H, m), 5.15 (1H, ddd, J=10, 10, 6 Hz), 5.89 (1H, s), 6.75-6.82 (3H, m), 7.09 (1H, d, J=10 Hz), 7.32-7.50 (5H, m), 7.58 (1H, d, J=10 Hz), 7.58-7.69 (4H, s);  
25 MASS (ES-): m/e 876 (M+Cl).

Example 98

Compound E98 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.5 Hz), 1.23-1.39 (4H, m), 30 1.29 (3x3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.71 (3H, m), 1.72-1.90 (3H, m), 2.08-2.24 (2H, m), 2.25-2.57 (4H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.19 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.55 (1H, d, J=4.5 Hz), 3.85 (2x3H, s), 3.85 (1H, m), 4.14-4.29 (2H, m), 4.67 (1H, m), 5.15 (1H, ddd, J=10, 10, 6 Hz), 5.88 (1H, s), 6.74-6.79 (3H, m), 7.12 (1H, d, J=10 Hz), 7.55 (1H, d, J=10 Hz);  
35 MASS (ES-): m/e 601;

$[\alpha]_D^{24} = -104.6^\circ$  ( $c=0.32$ ,  $\text{CHCl}_3$ ).

Example 99

Compound E99 was obtained in a manner similar to Example 1.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.87 (3H, d,  $J=7$  Hz), 0.88 (3H, t,  $J=7$  Hz),  
5 0.91 (3H, t,  $J=7$  Hz), 1.09 (3x3H, s), 1.12-1.24 (2H, m), 1.22 (3H, d,  
 $J=6.5$  Hz), 1.30 (3H, s), 1.38-1.52 (2H, m), 1.54-1.71 (1H, m), 1.74-  
2.10 (4H, m), 2.14-2.43 (6H, m), 3.53 (1H, m), 3.90 (1H, m), 4.21 (1H,  
m), 4.27 (1H, q,  $J=6.5$  Hz), 4.59 (1H, dd,  $J=10.5$ , 10.5 Hz), 4.77 (1H,  
m), 5.87 (1H, s), 6.61 (1H, d,  $J=15$ , 5 Hz), 6.86 (1H, dt,  $J=15.5$ , 7  
10 Hz), 7.19 (1H, d,  $J=10$  Hz), 7.30-7.49 (7H, m), 7.56-7.69 (4H, m);  
MASS (ES-)  $m/e$  743.

Example 100

Compound E100 was obtained in a manner similar to Example 4.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.86 (3H, d,  $J=7$  Hz), 0.88 (3H, t,  $J=7$  Hz),  
15 0.91 (3H, t,  $J=7$  Hz), 1.10 (3x3H, s), 1.16-1.28 (3H, m), 1.18 (3H, d,  
 $J=6.5$  Hz), 1.30 (3H, s), 1.37-1.70 (4H, m), 1.72-2.10 (4H, m), 2.11-  
2.43 (4H, m), 2.50 (2H, m), 3.53 (1H, dt,  $J=10$ , 7.5 Hz), 3.88 (1H, ddd,  
 $J=10$ , 10, 5 Hz), 4.18 (1H, m), 4.18 (1H, q,  $J=6.5$  Hz), 4.58 (1H, dd,  
 $J=10.5$ , 10.5 Hz), 4.75 (1H, m), 5.88 (1H, s), 7.13 (1H, d,  $J=10$  Hz),  
20 7.32-7.48 (7H, m), 7.57-7.70 (4H, m);  
MASS (ES-)  $m/e$  745.

Example 101

Compound E101 was obtained in a manner similar to Example 6.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.86 (3H, d,  $J=7$  Hz), 0.88 (3H, t,  $J=7$  Hz),  
25 0.91 (3H, t,  $J=7$  Hz), 1.06-1.40 (5H, m), 1.30 (3H, s), 1.38 (3H, d,  
 $J=6.5$  Hz), 1.50-2.10 (8H, m), 2.12-2.58 (6H, m), 3.53 (1H, dt,  $J=10$ ,  
7.5 Hz), 3.56 (1H, d,  $J=4.5$  Hz), 3.89 (1H, ddd,  $J=10$ , 10, 5 Hz), 4.14-  
4.29 (2H, m), 4.58 (1H, dd,  $J=10.5$ , 10.5 Hz), 4.76 (1H, dd,  $J=8$ , 1.5  
Hz), 5.91 (1H, s), 7.17 (1H, d,  $J=10.5$  Hz), 7.38 (1H, d,  $J=10.5$  Hz);  
30 MASS (ES-)  $m/e$  507;

$[\alpha]_D^{24} = -133.3^\circ$  ( $c=0.25$ ,  $\text{CHCl}_3$ ).

Example 102

Compound E102 was obtained in a manner similar to Example 1.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.84 (3H, d,  $J=6.6$  Hz), 0.86 (3H, t,  $J=7.3$   
35 Hz), 1.09 (3H, s), 1.22 (3H, d,  $J=6.6$  Hz), 1.32-2.02 (9H, m), 2.09-  
2.46 (4H, m), 2.78 (1H, dd,  $J=14.5$ , 8 Hz), 3.16 (1H, dd,  $J=14.5$ , 8 Hz),

3.51 (1H, m), 3.76 (3H, s), 4.03 (1H, m), 4.26 (1H, m), 4.27 (1H, q, J=6.6 Hz), 4.48 (1H, dd, J=10.5, 10.5 Hz), 4.69 (1H, m), 4.72 (1H, m), 6.28 (1H, d, J=10.5 Hz), 6.29 (1H, d, J=10 Hz), 6.58 (1H, d, J=15.5 Hz), 6.80 (2x1H, d, J=8.5 Hz), 6.83 (1H, dt, J=15, 5.7 Hz), 7.11 (2x1H, d, J=8.5 Hz), 7.22 (1H, d, J=10.5 Hz), 7.30-7.48 (6H, m), 7.55-7.69 (4H, m);

MASS (ES-) m/e 821.

#### Example 103

Compound E103 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, d, J=6.6 Hz), 0.86 (3H, d, J=7.3 Hz), 1.10 (3x3H, s), 1.13-2.02 (13H, m), 1.18 (3H, d, J=6.5 Hz), 2.25-2.52 (4H, m), 2.78 (1H, dd, J=14.2, 7.7 Hz), 3.15 (1H, dd, J=14.2, 7.7 Hz), 3.51 (1H, m), 3.76 (3H, s), 4.02 (1H, m), 4.18 (3H, q, J=6.5 Hz), 4.22 (1H, m), 4.48 (1H, dd, J=10.6, 10.5 Hz), 4.68 (1H, ddd, J=9.7, 7.7, 7.7 Hz), 4.72 (1H, m), 6.29 (1H, d, J=9.7 Hz), 6.30 (1H, d, J=10.5 Hz), 6.80 (2x1H, d, J=8.8 Hz), 7.11 (2x1H, d, J=8.8 Hz), 7.16 (1H, d, J=10.7 Hz), 7.31-7.48 (6H, m), 7.57-7.67 (4H, m);

MASS (ES-) m/e 823.

#### Example 104

Compound E104 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, d, J=6.6 Hz), 0.86 (3H, t, J=7.4 Hz), 1.09 (1H, m), 1.18-1.32 (4H, m), 1.37 (3H, d, J=6.8 Hz), 1.49-2.03 (8H, m), 2.26-2.55 (4H, m), 2.79 (1H, dd, J=14.5, 7.9 Hz), 3.15 (1H, dd, J=14.5, 7.7 Hz), 3.51 (1H, m), 3.57 (1H, d, J=4.5 Hz), 3.77 (3H, s), 4.02 (1H, m), 4.17-4.29 (2H, m), 4.48 (1H, dd, J=10.7, 10.6 Hz), 4.68 (1H, m), 4.73 (1H, m), 6.30 (2x1H, brd, J=10 Hz), 6.81 (2x1H, d, J=8.5 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.20 (1H, d, J=10.6 Hz);

MASS (ES-) m/e 585;

$[\alpha]_D^{30} = -61.5^\circ$  (c=0.33, CHCl<sub>3</sub>)

#### Example 105

Compound E105 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (3x3H, s), 1.24 (3H, d, J=7 Hz), 1.43 (2H, m), 1.61-1.89 (4H, m), 2.10-2.40 (4H, m), 2.77 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13.5, 5 Hz), 3.08 (1H, m), 3.16 (1H, dd, J=14, 8 Hz), 3.18 (1H, dd, J=13.5, 11 Hz), 3.77 (3H, s), 3.94 (1H, m), 4.27 (1H, m), 4.27 (1H, q, J=7 Hz), 4.61 (1H, dd, J=8, 2.5 Hz), 4.69 (1H,

ddd, J=10, 8, 7 Hz), 5.16 (1H, ddd, J=11, 10, 5 Hz), 6.30 (1H, d, J=10 Hz), 6.59 (1H, brd, J=16 Hz), 6.81 (2x1H, d, J=8.5 Hz), 6.84 (1H, dt, J=16, 7 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.12-7.48 (14H, m), 7.56-7.69 (4H, m);

5 MASS (ES-) m/e 855.

Example 106

Compound E106 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.14-1.30 (4H, m), 1.18 (3H, d, J=7 Hz), 1.36-1.82 (6H, m), 2.10-2.40 (2H, m), 2.49 (2H, m), 2.77 (1H, dd, J=14.5, 7 Hz), 2.87 (1H, dd, J=13, 5.5 Hz), 3.02-3.24 (3H, m), 3.77 (3H, s), 3.94 (1H, m), 4.18 (1H, q, J=7 Hz), 4.24 (1H, m), 4.61 (1H, m), 4.69 (1H, m), 5.06 (1H, ddd, J=10, 10, 5.5 Hz), 6.29 (1H, d, J=9.5 Hz), 6.46 (1H, d), 6.81 (2x1H, d, J=9 Hz), 7.09-7.30 (8H, m), 7.32-7.48 (6H, m), 7.58-7.68 (4H, m);

15 MASS (ES-) m/e 857.

Example 107

Compound E107 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.20-1.36 (4H, m), 1.38 (3H, d, J=7 Hz), 1.54-1.88 (6H, m), 2.12-2.56 (4H, m), 2.78 (1H, dd, J=14.5, 7 Hz), 2.87 (1H, dd, J=13.5, 5.5 Hz), 3.02-3.24 (3H, m), 3.56 (1H, d, J=5 Hz), 3.94 (1H, m), 4.17-4.30 (2H, m), 4.61 (1H, m), 4.68 (1H, m), 5.06 (1H, ddd, J=10, 10, 5.5 Hz), 6.32 (1H, d, J=10 Hz), 6.46 (1H, d, J=10 Hz), 6.82 (2x1H, d, J=8.5 Hz), 7.08-7.32 (8H, m);

MASS (ES-) m/e 619;

25  $[\alpha]_D^{30} = -60.9^\circ$  (C=0.31, CHCl<sub>3</sub>).

Example 108

Compound E108 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.91 (3H, t, J=7.5 Hz), 1.09 (3H, s), 1.22 (3H, d, J=7 Hz), 1.36 (3H, s), 1.46 (2H, m), 1.56-1.72 (1H, m), 1.78-2.04 (3H, m), 2.12-2.54 (6H, m), 3.74 (1H, m), 4.04 (1H, m), 4.21-4.32 (2H, m), 4.75 (1H, m), 5.98 (1H, s), 6.19 (1H, d, J=10 Hz), 6.61 (1H, brd, J=16 Hz), 6.86 (1H, dt, J=16, 7 Hz), 7.16 (1H, d, J=10 Hz), 7.24-7.49 (11H, m), 7.56-7.68 (4H, m), 8.08 (1H, d, J=10 Hz);

MASS (ES-) m/e 763.

35 Example 109

Compound E109 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.91 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=7 Hz), 1.18-1.30 (4H, m), 1.36 (3H, s), 1.38-2.06 (6H, m), 2.09-2.58 (6H, m), 3.74 (1H, m), 4.03 (1H, m), 4.18 (1H, q, J=7 Hz), 4.26 (1H, m), 4.75 (1H, dd, J=8, 2 Hz), 5.98 (1H, s), 6.18 (1H, d, J=10 Hz), 7.10 (1H, d, J=10.5 Hz), 7.28-7.49 (11H, m), 7.58-7.69 (4H, m), 8.12 (1H, d, J=10 Hz);  
MASS (ES-) m/e 765.

#### Example 110

Compound E110 was obtained in a manner similar to Example 6.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.92 (3H, t, J=7.3 Hz), 1.24-1.40 (4H, m), 1.36 (3H, s), 1.38 (3H, d, J=7 Hz), 1.53-1.68 (2H, m), 1.73-2.57 (10H, m), 3.55 (1H, d, J=5 Hz), 3.74 (1H, m), 4.04 (1H, m), 4.17-4.30 (2H, m), 4.76 (1H, dd, J=8.2 Hz), 5.99 (1H, s), 6.19 (1H, d, J=10.3 Hz), 7.14 (1H, d, J=10.6 Hz), 7.25-7.42 (5H, m), 8.10 (1H, d, J=10.3 Hz);  
15 MASS (ES-) m/e 527;  
[α]<sub>D</sub><sup>30</sup> = -174.4° (c=0.22, CHCl<sub>3</sub>).

#### Example 111

Compound E111 was obtained in a manner similar to Example 1.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.5 Hz), 0.96 (2H, m), 1.09 (3x3H, s), 1.12-1.32 (2H, m), 1.22 (3H, d, J=7 Hz), 1.29 (3H, s), 1.36-1.51 (2H, m), 1.54-2.00 (13H, m), 2.10-2.44 (6H, m), 3.52 (1H, dt, J=10, 7 Hz), 3.96 (1H, m), 4.21 (1H, dt, J=10, 7.5 Hz), 4.26 (1H, q, J=7 Hz), 4.74 (1H, dt, J=8, 2 Hz), 5.00 (1H, d, J=10, 8 Hz), 5.85 (1H, s), 6.81 (1H, d, J=16 Hz), 6.86 (1H, dt, J=16, 7 Hz), 7.14 (1H, d, J=10 Hz), 7.30-7.50 (7H, m), 7.56-7.69 (4H, m);  
25 MASS (ES-) m/e 783.

#### Example 112

Compound E112 was obtained in a manner similar to Example 4.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 0.96 (2H, m), 1.10 (3x3H, s), 1.13-1.34 (6H, m), 1.18 (3H, d, J=6.5 Hz), 1.29 (3H, s), 1.45 (2H, m), 1.52-2.00 (13H, m), 2.08-2.43 (4H, m), 2.50 (2H, m), 3.52 (1H, dt, J=10.5, 7 Hz), 3.96 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=6.5 Hz), 4.74 (1H, dd, J=8, 2 Hz), 5.00 (1H, dd, J=10, 7.5 Hz), 5.85 (1H, s), 7.09 (1H, d, J=10 Hz), 7.31-7.48 (7H, m), 7.57-7.67 (4H, m);  
35 MASS (ES-) m/e 785.

#### Example 113

Compound E113 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.3 Hz), 0.96 (2H, m), 1.08-1.40 (8H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.2 Hz), 1.50-2.00 (13H, m), 2.08-2.57 (6H, m), 3.52 (1H, ddd, J=10, 7.5, 7 Hz), 3.56 (1H, d, J=5 Hz), 3.96 (1H, m), 4.13-4.28 (2H, m), 4.74 (1H, dd, J=8, 2 Hz), 4.99 (1H, dt, J=10, 8 Hz), 5.88 (1H, s), 7.12 (1H, d, J=10 Hz), 7.34 (1H, d, J=10 Hz);

MASS (ES-) m/e 547.

Example 114

10 Compound E114 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.3 Hz), 0.86 (3H, t, J=7.3 Hz), 0.96 (2H, m), 1.10 (3x3H, m), 1.17 (2H, m), 1.42 (2H, m), 1.52-2.00 (15H, m), 2.10-2.44 (6H, m), 3.52 (1H, dt, J=10, 7 Hz), 3.96 (1H, m), 4.15 (1H, t, J=6 Hz), 4.20 (1H, dt, J=10.5, 7.5 Hz), 4.74 (1H, dd, J=8, 2 Hz), 5.00 (1H, dt, J=10, 8 Hz), 5.85 (1H, s), 6.54 (1H, brd, J=16 Hz), 6.79 (1H, dt, J=16, 7 Hz), 7.14 (1H, d, J=10.5 Hz), 7.28-7.48 (7H, m), 7.54-7.68 (4H, m);

MASS (ES-) m/e 797.

Example 115

20 Compound E115 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 0.86 (3H, t, J=7.3 Hz), 0.96 (2H, m), 1.11 (3x3H, s), 1.12-1.27 (6H, m), 1.29 (3H, s), 1.37 (2H, m), 1.47-1.98 (15H, m), 2.07-2.49 (6H, m), 3.52 (1H, dt, J=10, 7 Hz), 3.95 (1H, m), 4.10 (1H, t, J=7 Hz), 4.16 (1H, dt, J=10, 7 Hz), 4.73 (1H, dd, J=8, 2 Hz), 4.99 (1H, dt, J=10, 7 Hz), 5.84 (1H, s), 7.08 (1H, d, J=10 Hz), 7.32-7.48 (7H, m), 7.58-7.66 (4H, m);

MASS (ES+): m/e 799.

Example 116

Compound E116 was obtained in a manner similar to Example 6.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.3 Hz), 0.94 (3H, t, J=7 Hz), 0.94 (2H, m), 1.08-1.40 (8H, m), 1.29 (3H, s), 1.50-2.00 (15H, m), 2.07-2.50 (6H, m), 3.49 (1H, d, J=4.5 Hz), 3.52 (1H, m), 3.96 (1H, m), 4.10-4.25 (2H, m), 4.74 (1H, dd, J=7.5, 2 Hz), 4.99 (1H, dt, J=10, 7.5 Hz), 5.88 (1H, s), 7.12 (1H, d, J=10 Hz), 7.34 (1H, d, J=10 Hz);

35 MASS (ES-) m/e 561.

Example 117

Compound E117 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (3x3H, s), 1.22 (3H, d, J=7 Hz), 1.24-1.92 (14H, m), 1.96-2.39 (5H, m), 2.62 (1H, m), 2.95 (1H, dd, J=13.5, 6 Hz), 3.21 (1H, m), 3.25 (1H, dd, J=13.5, 10 Hz), 3.93 (1H, m), 4.22 (1H, m), 4.27 (1H, q, J=7 Hz), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.74 (1H, s), 6.62 (1H, d, J=16 Hz), 6.87 (1H, dt, J=16, 7 Hz), 7.15-7.29 (6H, m), 7.29-7.48 (7H, m), 7.56-7.68 (4H, m);  
MASS (ES-) m/e 804.

Example 118

10 Compound E118 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.18 (3H, d, J=7 Hz), 1.20-1.68 (14H, m), 1.69-1.92 (4H, m), 2.04 (1H, m), 2.18 (1H, m), 2.32 (1H, m), 2.51 (2H, m), 2.63 (1H, m), 2.95 (1H, dd, J=14, 6 Hz), 3.21 (1H, m), 3.25 (1H, dd, J=14, 10 Hz), 3.92 (1H, m), 4.18 (1H, q, J=7 Hz), 4.20 (1H, m), 4.66 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.73 (1H, s), 7.13 (1H, s), 7.17-7.31 (5H, m), 7.33-7.48 (7H, m), 7.59-7.68 (4H, m);  
MASS (ES-) m/e 805.

Example 119

20 Compound E119 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.20-1.92 (19H, m), 1.94-2.70 (5H, m), 2.95 (1H, dd, J=13.5, 6 Hz), 3.20 (1H, m), 3.24 (1H, dd, J=13.5, 10 Hz), 3.56 (1H, d, J=4.5 Hz), 3.92 (1H, m), 4.15-4.29 (2H, m), 4.64 (1H, m), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.75 (1H, s), 7.17 (1H, d, J=10 Hz), 7.19-7.32 (5H, m), 7.38 (1H, d, J=10 Hz);  
MASS (ES-) m/e 567;  
[α]<sub>D</sub><sup>25</sup> = -98.8° (c=0.33, CHCl<sub>3</sub>).

Example 120

Compound E120 was obtained in a manner similar to Example 1.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 1.11 (3x3H, s), 1.23-1.93 (16H, m), 1.96-2.37 (5H, m), 2.64 (1H, m), 2.96 (1H, dd, J=13, 6 Hz), 3.15-3.31 (2H, m), 3.93 (1H, m), 4.16 (1H, t, J=6 Hz), 4.22 (1H, m), 4.66 (1H, m), 5.17 (1H, m), 5.72 (1H, s), 6.56 (1H, d, J=16 Hz), 6.81 (1H, dt, J=16, 7 Hz), 7.15-7.48 (13H, m), 7.55-7.69 (4H, m);  
MASS (ES+): m/e 819.

Example 121

Compound E121 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.11 (3x3H, s),  
1.14-1.90 (20H, m), 1.95-2.23 (2H, m), 2.26-2.49 (3H, m), 2.64 (1H, m),  
5 2.95 (1H, dd, J=13.5, 6 Hz), 3.21 (1H, m), 3.25 (1H, dd, J=13.5, 10  
Hz), 3.91 (1H, m), 4.11 (1H, t, J=6 Hz), 4.18 (1H, m), 4.66 (1H, m),  
5.16 (1H, ddd, J=10, 10, 6 Hz), 5.69 (1H, s), 7.12 (1H, d, J=10 Hz),  
7.16-7.31 (5H, m), 7.32-7.48 (7H, m), 7.57-7.67 (4H, m);

MASS (ES<sup>+</sup>): m/e 819.

10 Example 122

Compound E122 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.94 (3H, t, J=7.4 Hz), 1.20-1.95 (20H, m),  
2.03 (1H, m), 2.16 (1H, m), 2.31 (1H, m), 2.44 (2H, m), 2.62 (1H, m),  
2.95 (1H, dd, J=14, 6 Hz), 3.14-3.30 (2H, m), 3.49 (1H, d, J=5 Hz),  
15 3.92 (1H, m), 4.08-4.26 (2H, m), 4.68 (1H, m), 5.16 (1H, ddd, J=10, 10,  
6 Hz), 5.72 (1H, s), 7.12-7.31 (5H, m), 7.16 (1H, d, J=10 Hz), 7.38  
(1H, d, J=10 Hz);

MASS (ES<sup>-</sup>) m/e 581;

[α]<sub>D</sub><sup>25</sup> = -100.4° (c=0.30, CHCl<sub>3</sub>).

20 Example 123

Compound E123 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.90 (2H, m), 1.06-1.32 (4H, m), 1.10 (9H,  
s), 1.23 (3H, d, J=7 Hz), 1.36-1.52 (3H, m), 1.56-1.82 (10H, m), 2.14-  
2.39 (4H, m), 2.94 (1H, dd, J=14, 5 Hz), 3.10 (1H, m), 3.23 (1H, dd,  
25 J=14, 10 Hz), 3.94 (1H, m), 4.27 (1H, m), 4.27 (1H, q, J=7 Hz), 4.52  
(1H, m), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10, 5 Hz), 6.04 (1H, d,  
J=10 Hz), 6.48 (1H, d, J=10 Hz), 6.61 (1H, d, J=16 Hz), 6.87 (1H, dt,  
J=16, 7 Hz), 7.16-7.50 (12H, m), 7.57-7.70 (4H, m);

MASS (ES<sup>+</sup>): m/e 855.

30 Example 124

Compound E124 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.92 (2H, m), 1.08-1.32 (8H, m), 1.10 (9H,  
s), 1.19 (3H, d, J=7 Hz), 1.38-1.50 (3H, m), 1.58-1.84 (10H, m), 2.19  
(2H, m), 2.32 (2H, m), 2.51 (2H, brt, J=7 Hz), 2.94 (1H, dd, J=13, 5  
35 Hz), 3.10 (1H, m), 3.23 (1H, dd, J=13, 10 Hz), 3.93 (1H, m), 4.18 (1H,  
q, J=7 Hz), 4.25 (1H, dt, J=10, 7 Hz), 4.52 (1H, dt, J=11, 8 Hz), 4.62

(1H, m), 5.09 (1H, ddd, J=10, 10, 5 Hz), 6.06 (1H, d, J=10 Hz), 6.51 (1H, d, J=11 Hz), 7.13 (1H, d, J=10 Hz), 7.18-7.32 (5H, m), 7.34-7.48 (6H, m), 7.59-7.67 (4H, m);

MASS (ES-) m/e 833.

5 Example 125

Compound E125 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.92 (1H, m), 1.07-1.50 (10H, m), 1.38 (3H, d, J=7 Hz), 1.54-1.90 (11H, m), 2.18 (1H, m), 2.33 (1H, m), 2.46 (2H, m), 2.93 (1H, dd, J=13, 5 Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13, 10 Hz), 3.56 (1H, d, J=5 Hz), 3.93 (1H, m), 4.18-4.31 (2H, m), 4.52 (1H, dt, J=10, 7 Hz), 4.62 (1H, m), 5.08 (1H, ddd, J=10, 10, 5 Hz), 6.08 (1H, d, J=10 Hz), 6.49 (1H, d, J=10 Hz), 7.16 (1H, d, J=10 Hz), 7.17-7.32 (5H, m);

MASS (ES-) m/e 595;

15  $[\alpha]_D^{23} = -53.8^\circ$  (c=0.09, CHCl<sub>3</sub>).

Example 126

Compound E126 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7 Hz), 0.90 (2H, m), 1.04-1.32 (4H, m), 1.10 (9H, s), 1.36-1.50 (3H, m), 1.52-1.90 (12H, m), 2.10-2.36 (4H, m), 2.96 (1H, dd, J=13, 5 Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13, 10 Hz), 3.93 (1H, m), 4.15 (1H, t, J=6 Hz), 4.27 (1H, ddd, J=10, 8, 7 Hz), 4.52 (1H, ddd, J=10, 8, 7 Hz), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10, 5 Hz), 6.05 (1H, d, J=10 Hz), 6.48 (1H, d, J=10 Hz), 6.53 (1H, d, J=16 Hz), 6.79 (1H, dt, J=16, 7 Hz), 7.14-7.47 (12H, m), 7.54-7.68 (4H, m);

MASS (ES-) m/e 845.

Example 127

Compound E127 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7 Hz), 0.90 (2H, m), 1.11 (9H, s), 1.12-1.82 (23H, m), 2.15-2.47 (4H, m), 2.94 (1H, dd, J=13, 5 Hz), 3.10 (1H, m), 3.22 (1H, dd, J=13, 10 Hz), 3.93 (1H, m), 4.11 (1H, t, J=6 Hz), 4.24 (1H, dt, J=10, 7 Hz), 4.52 (1H, dt, J=10, 7 Hz), 4.62 (1H, m), 5.09 (1H, ddd, J=10, 10, 5 Hz), 6.06 (1H, d, J=10 Hz), 6.51 (1H, d, J=10 Hz), 7.12 (1H, d, J=10 Hz), 7.18-7.32 (5H, m), 7.33-7.47 (6H, m), 7.58-7.66 (4H, m);

MASS (ES-) m/e 847.

Example 128

Compound E128 was obtained in a manner similar to Example 6.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80-1.00 (2H, m), 0.94 (3H, t, J=7 Hz),  
1.06-1.96 (23H, m), 2.18 (1H, m), 2.31 (1H, m), 2.44 (2H, m), 2.93 (1H,  
5 dd, J=13, 5 Hz), 3.09 (1H, m), 3.22 (1H, dd, J=13, 10 Hz), 3.51 (1H, d,  
J=5 Hz), 3.93 (1H, m), 4.15 (1H, m), 4.26 (1H, dt, J=10, 8 Hz), 4.52  
(1H, dt, J=10, 7 Hz), 4.62 (1H, m), 5.08 (1H, ddd, J=10, 10, 5 Hz),  
6.08 (1H, d, J=10 Hz), 6.50 (1H, d, J=10 Hz), 7.16 (1H, d, J=10 Hz),  
7.16-7.33 (5H, m);  
10 MASS (ES-) m/e 609;  
[α]<sub>D</sub><sup>23</sup> = -49.6° (c=0.26, CHCl<sub>3</sub>).

Example 129

Compound E129 was obtained in a manner similar to Example 1.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.90 (2H, m), 1.09 (9H, s), 1.11-1.33 (8H,  
15 m), 1.22 (3H, d, J=7 Hz), 1.36-1.52 (3H, m), 1.59-1.90 (6H, m), 2.14-  
2.38 (4H, m), 2.94 (1H, dd, J=13, 5 Hz), 3.10 (1H, m), 3.22 (1H, dd,  
J=13, 6 Hz), 3.94 (1H, m), 4.22-4.33 (2H, m), 4.52 (1H, dt, J=8, 7 Hz),  
4.62 (1H, m), 5.09 (1H, ddd, J=10, 6, 5 Hz), 6.04 (1H, d, J=10 Hz),  
6.48 (1H, d, J=10 Hz), 6.60 (1H, d, J=16 Hz), 6.86 (1H, dt, J=16, 7  
20 Hz), 7.15-7.48 (12H, m);  
MASS (ES+): m/e 833.

Example 130

Compound E130 was obtained in a manner similar to Example 4.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.89 (2H, m), 1.05-1.34 (8H, m), 1.10 (9H,  
25 s), 1.18 (3H, d, J=7 Hz), 1.37-1.52 (3H, m), 1.58-1.85 (10H, m), 2.12-  
2.38 (2H, m), 2.50 (2H, m), 2.93 (1H, dd, J=13, 5 Hz), 3.10 (1H, m),  
3.22 (1H, dd, J=13, 11 Hz), 3.93 (1H, m), 4.18 (1H, q, J=7 Hz), 4.24  
(1H, dt, J=10, 8 Hz), 4.52 (1H, dt, J=10, 7 Hz), 4.62 (1H, m), 5.08  
(1H, ddd, J=11, 10, 5 Hz), 6.06 (1H, d, J=10 Hz), 6.50 (1H, d, J=10  
30 Hz), 7.12 (1H, d, J=10 Hz), 7.17-7.32 (5H, m), 7.33-7.48 (6H, m),  
7.58-7.67 (4H, m);  
MASS (ES-) m/e 833.

Example 131

Compound E131 was obtained in a manner similar to Example 6.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.90 (2H, m), 1.06-1.90 (21H, m), 1.38 (3H,  
35 d, J=7 Hz), 2.18 (1H, m), 2.27-2.58 (3H, m), 2.93 (1H, dd, J=13, 5 Hz),

3.10 (1H, m), 3.22 (1H, dd, J=13, 10 Hz), 3.58 (1H, brd, J=3 Hz), 3.93 (1H, m), 4.18-4.32 (2H, m), 4.52 (1H, dt, J=10, 8 Hz), 4.62 (1H, m), 5.08 (1H, ddd, J=10, 10, 5 Hz), 6.12 (1H, d, J=10 Hz), 6.51 (1H, d, J=10 Hz), 7.13-7.33 (6H, m);

5 MASS (ES-) m/e 595;

$[\alpha]_D^{23} = -46.4^\circ$  (c=1.39, CHCl<sub>3</sub>).

#### Example 132

Compound E132 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.5 Hz), 0.87 (3H, t, J=7.5 Hz), 1.10 (9H, s), 1.29 (3H, s), 1.42 (2H, m), 1.54-1.69 (3H, m), 1.74-1.92 (3H, m), 1.98-2.42 (8H, m), 2.65 (1H, m), 3.32 (1H, m), 3.75 (1H, m), 4.15 (1H, t, J=6 Hz), 4.21 (1H, m), 4.72 (1H, m), 4.85 (1H, m), 5.83 (1H, s), 6.54 (1H, d, J=16 Hz), 6.80 (1H, dt, J=16, 7 Hz), 7.11 (1H, d, J=10 Hz), 7.15-7.23 (3H, m), 7.25-7.47 (9H, m), 7.55-7.67 (4H, m);

15 MASS (ES+): m/e 829.

#### Example 133

Compound E133 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 0.87 (3H, t, J=7.3 Hz), 1.11 (9H, s), 1.14-1.25 (4H, m), 1.28 (3H, s), 1.37 (2H, m), 1.48-1.92 (6H, m), 2.00-2.25 (4H, m), 2.26-2.49 (4H, m), 2.64 (2H, m), 3.32 (1H, m), 3.76 (1H, m), 4.10 (1H, t, J=6 Hz), 4.17 (1H, dt, J=10, 7 Hz), 4.72 (1H, m), 4.84 (1H, dt, J=10, 7 Hz), 5.82 (1H, s), 7.05 (1H, d, J=10 Hz), 7.14-7.22 (3H, m), 7.24-7.48 (9H, m), 7.57-7.66 (4H, m);

25 MASS (ES-) m/e 807.

#### Example 134

Compound E134 was obtained in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.88 (3H, t, J=7 Hz), 0.94 (3H, t, J=7 Hz), 1.22-1.40 (4H, m), 1.29 (3H, s), 1.52-1.70 (4H, m), 1.74-1.98 (4H, m), 2.01-2.26 (4H, m), 2.29-2.50 (4H, m), 2.65 (2H, m), 3.33 (1H, m), 3.50 (1H, d, J=5 Hz), 3.75 (1H, m), 4.08-4.26 (2H, m), 4.73 (1H, m), 4.85 (1H, ddd, J=10, 8, 7 Hz), 5.84 (1H, s), 7.09 (1H, d, J=10 Hz), 7.15-7.24 (3H, m), 7.25-7.33 (2H, m), 7.42 (1H, d, J=10 Hz);

MASS (ES-) m/e 569.

#### Example 135

Compound E135 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.5 Hz), 1.09 (9H, s), 1.21 (3H, d, J=7 Hz), 1.29 (3H, s), 1.45 (2H, m), 1.64 (1H, m), 1.75-1.92 (3H, m), 2.00-2.42 (8H, m), 2.65 (2H, m), 3.32 (1H, m), 3.75 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7 Hz), 4.72 (1H, m), 4.85 (1H, dt, J=10, 7.5 Hz), 5.83 (1H, s), 6.61 (1H, d, J=16 Hz), 6.86 (1H, dt, J=16, 7 Hz), 7.11 (1H, d, J=10 Hz), 7.15-7.23 (3H, m), 7.24-7.49 (9H, m), 7.56-7.69 (4H, m);  
MASS (ES+) m/e 815.

Example 136

10 Compound E136 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7 Hz), 1.10 (9H, s), 1.18 (3H, d, J=7 Hz), 1.20-1.32 (4H, m), 1.28 (3H, s), 1.38-1.52 (3H, m), 1.72-1.91 (3H, m), 2.00-2.42 (6H, m), 2.50 (2H, m), 2.64 (2H, m), 3.34 (1H, m), 3.74 (1H, m), 4.18 (1H, q, J=7 Hz), 4.18 (1H, m), 4.72 (1H, m), 4.84 (1H, m), 5.83 (1H, s), 7.05 (1H, d, J=10 Hz), 7.14-7.22 (3H, m), 7.24-7.32 (2H, m), 7.33-7.49 (7H, m), 7.58-7.67 (4H, m);  
MASS (ES-) m/e 793.

Example 137

Compound E137 was obtained in a manner similar to Example 6.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.87 (3H, t, J=7.5 Hz), 1.20-1.40 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7 Hz), 1.53-1.69 (3H, m), 1.75-1.92 (3H, m), 1.98-2.25 (4H, m), 2.26-2.55 (4H, m), 2.64 (2H, m), 3.32 (1H, m), 3.56 (1H, d, J=4.5 Hz), 3.74 (1H, m), 4.10-4.29 (2H, m), 4.72 (1H, m), 4.84 (1H, ddd, J=10, 7.5, 7.5 Hz), 5.84 (1H, s), 7.08 (1H, d, J=10 Hz), 7.12-7.23 (3H, m), 7.24-7.33 (2H, m), 7.42 (1H, d, J=10 Hz);  
MASS (ES-) m/e 555.

Example 138

Compound E138 was obtained in a manner similar to the method disclosed in WO00/21979.

30 Example 139

To a stirred solution of Compound E138 (506 mg) in methanol (10 ml) was added aqueous sodium periodate (1.08 M, 2ml) at ambient temperature and the resulting mixture was stirred at the same temperature overnight. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate and 1N hydrochloric acid. The organic layer was separated, washed with brine, dried over

sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography eluting with 5% methanol/chloroform (v/v) as a solvent mixture to give the Compound E139 (480 mg) as a white amorphous solid.

5 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 0.88 (3H, d, J=6.5 Hz), 1.20-1.42 (5H, m), 1.28 (3H, s), 1.53-1.70 (3H, m), 1.81 (1H, m), 2.17 (1H, m), 2.24-2.42 (4H, m), 2.62 (1H, m), 2.73 (1H, dd, J=9.5 and 8 Hz), 2.96 (1H, dd, J=13.5, 6 Hz), 3.23 (1H, dd, J=13.5, 10 Hz), 4.05 (1H, dd, J=9.5, 7.5 Hz), 4.23 (1H, m), 4.69 (1H, dd, J=8.2 Hz), 5.16  
10 (1H, ddd, J=10, 10, 6 Hz), 6.10 (1H, s), 7.16-7.32 (6H, m), 7.60 (1H, d, J=10 Hz);

MASS (ES<sup>+</sup>): m/e 529.

#### Example 140

To a stirred solution of Compound E138 (1000 mg) in methanol  
15 (20 ml) was added aqueous solution of sodium periodate (1.08 M, 2 ml) at ambient temperature and the resulting mixture was stirred at the same temperature overnight. The solution was concentrated in vacuo and the residue was dissolved in ethyl acetate and added 1 N  
hydrochloric acid. The organic layer was separated, washed with brine,  
20 dried over sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by flash chromatography using 5% methanol/chloroform (v/v) as a solvent mixture to give the Compound E140 (949 mg) as a white amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 0.87 (3H, d, J=7  
25 Hz), 1.21-1.45 (5H, m), 1.28 (3H, s), 1.53-1.70 (3H, m), 1.82 (1H, m), 2.17 (1H, m), 2.25-2.42 (4H, m), 2.62 (1H, m), 2.72 (1H, dd, J=9, 8 Hz), 2.96 (1H, dd, J=13, 6 Hz), 3.23 (1H, dd, J=13, 10 Hz), 4.05 (1H, dd, J=9, 7 Hz), 4.22 (1H, m), 4.68 (1H, dd, J=7, 2 Hz), 5.15 (1H, ddd, J=10, 9, 6 Hz), 6.04 (1H, s), 7.15-7.32 (6H, m), 7.58 (1H, d, J=9 Hz);  
30 MASS (ES<sup>+</sup>): m/e 529.

#### Example 141

To a stirred solution of Compound E140 in dichloromethane (2  
ml) was added N-methylhydroxylamine hydrochloride (18 mg), 1-  
hydroxybenzotriazole (58.2 mg) and a solution of 1-ethyl-3-(3'-  
35 dimethylaminopropyl)carbodiimide (67.0 mg) in dichloromethane at ambient temperature and the resulting mixture was stirred at the same

temperature for three days. This mixture was poured into water and the organic layer was separated. The organic layer was washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography using 9% methanol/chloroform (v/v) as a solvent mixture to give the Compound E141 (18 mg) as a white amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 0.88 (3H, d, J=6.5 Hz), 1.20-1.44 (5H, m), 1.28 (3H, s), 1.52-1.90 (5H, m), 2.15 (1H, m), 2.25-2.42 (3H, m), 2.62 (1H, m), 2.73 (1H, dd, J=9.5, 7.5 Hz), 2.82 (1H, s), 2.96 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 10 Hz), 4.06 (1H, dd, J=9.5, 8 Hz), 4.19 (1H, dt, J=10, 7.5 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.16 (1H, ddd, J=10, 10, 6 Hz), 5.83 (1H, s), 7.16 (1H, d, J=10 Hz), 7.19-7.33 (5H, m), 7.54 (1H, d, J=10 Hz);

MASS (ES-) m/e 556;

[α]<sub>D</sub><sup>21</sup> = -130.8° (c=0.30, CHCl<sub>3</sub>).

#### Example 142

To a stirred solution of Compound E139 (473 mg) in dichloromethane (5 ml) was added 1-hydroxybenzotriazole (181 mg), a solution of 1-ethyl-3-(3'-dimethylaminopropyl)carbodiimide (208 mg) in chloroform and N, O-dimethylhydroxylamine hydrochloric acid (131 mg) at ambient temperature and the resulting mixture was left at the same temperature for two weeks. This mixture was poured into 10% aqueous solution of citric acid and the organic layer was separated, washed with saturated aqueous sodium bicarbonate solution and brine. The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by flash chromatography eluting with ethyl acetate as an eluting solvent to give the Compound E142 (453 mg) as a white amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 0.88 (3H, d, J=6.6 Hz), 1.25-1.44 (6H, m), 1.29 (3H, s), 1.55-1.69 (2H, m), 1.83 (1H, m), 2.14 (1H, m), 2.26-2.45 (4H, m), 2.65 (1H, m), 2.73 (1H, dd, J=9.5, 8 Hz), 2.96 (1H, dd, J=13.5, 6 Hz), 3.18 (3H, s), 3.24 (1H, dd, J=13.5, 10 Hz), 3.68 (3H, s), 4.06 (1H, dd, J=9.5, 7.3 Hz), 4.21 (1H, m), 4.67 (1H, dd, J=8, 2 Hz), 5.16 (1H, ddd, J=10.3, 10, 6 Hz), 5.81 (1H, s), 7.14 (1H, d, J=10.2 Hz), 7.16-7.32 (5H, m), 7.56 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 572.

Example 143

To a stirred solution of the Compound E142 (97 mg) in tetrahydrofuran (4 ml) was added ethyl magnesium bromide (1.04 M in tetrahydrofuran, 1.6 ml) dropwise at -78°C and the mixture was allowed  
5 to warm to 0°C. The reaction mixture was quenched with saturated aqueous sodium bicarbonate solution at ambient temperature and the resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by  
10 preparative thin layer chromatography using 90% ethyl acetate/hexane (v/v) as a solvent mixture to give the Compound E143 (38 mg) as a white amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 0.88 (3H, d, J=6.6 Hz), 1.05 (3H, t, J=7.3 Hz), 1.20-1.44 (6H, m), 1.28 (3H, s), 1.48-  
15 1.71 (3H, m), 1.81 (1H, m), 2.14 (1H, m), 2.26-2.46 (5H, m), 2.63 (1H, m), 2.73 (1H, dd, J=9.5, 8 Hz), 2.96 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 10 Hz), 4.06 (1H, dd, J=9.5, 7.5 Hz), 4.19 (1H, dt, J=10, 7.5 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.16 (1H, ddd, J=10, 10.6 Hz), 5.79 (1H, s), 7.14 (1H, d, J=10 Hz), 7.18-7.32 (5H, m), 7.54 (1H, d, J=10  
20 Hz);

MASS (ES<sup>+</sup>): m/e 541.

Example 144

To a stirred solution of dimethyl 3-fluoro-2-oxopropylphosphonate (86.1 mg) in 2-propanol (3 ml) was added cesium  
25 carbonate (152 mg) at ambient temperature and the mixture was stirred at the same temperature for half an hour. To the resulting light yellow solution was added a solution of the starting compound (Compound (105)) (200 mg) in isopropyl alcohol at the same temperature and the mixture was stirred at the same temperature for two hours.  
30 The reaction mixture was quenched with 10% aqueous solution of citric acid, diluted with ethyl acetate and water. The organic layer was separated and washed with saturated sodium bicarbonate solution and brine. The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by  
35 preparative thin layer chromatography using 66% ethyl acetate/hexane (v/v) as a solvent mixture to give Compound E144 (68 mg) as a white

amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7 Hz), 1.29 (3H, s), 1.50 (2H, m), 1.64-1.92 (4H, m), 2.08-2.40 (6H, m), 2.97 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.85 (1H, m), 4.24 (1H, ddd, J=10, 7.5, 7 Hz), 4.67 (1H, m), 4.96 (2H, d, J=48 Hz), 5.19 (1H, ddd, J=10.5, 9.5, 6 Hz), 5.82 (1H, s), 6.36 (1H, m), 7.00 (1H, ddd, J=16, 7, 7 Hz), 7.15 (1H, d, J=10 Hz), 7.17-7.32 (5H, m), 7.50 (1H, d, J=10.5 Hz);

MASS (ES-) m/e 527;

10 [α]<sub>D</sub><sup>23</sup> = -90.7 (c=0.25, CHCl<sub>3</sub>).

Example 145

To a stirred solution of dimethyl 3-fluoro-2-oxopropylphosphonate (356 mg) in 2-propanol (10 ml) was added cesium carbonate (599 mg) at 0°C and the mixture was stirred at ambient temperature for half an hour. To the resulting yellow brown solution was added a solution of the starting compound (Compound (81)) (484 mg) in tetrahydrofuran (5 ml) and 2-propanol (5 ml) at the same temperature and the resulting mixture was stirred for half an hour at the same temperature. The reaction mixture was quenched with 10% aqueous solution of citric acid, diluted with ethyl acetate and water. The organic layer was separated and washed with water and brine. The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using ethyl acetate to give the Compound E145 (320 mg) as a white amorphous solid.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 1.29 (3H, s), 1.40-1.90 (6H, m), 2.08-2.40 (6H, m), 2.89 (1H, dd, J=14, 6 Hz), 3.18 (1H, dd, J=14, 10 Hz), 3.26 (1H, m), 3.77 (3H, s), 3.86 (1H, m), 4.22 (1H, dt, J=10, 7.5 Hz), 4.67 (1H, m), 4.96 (2H, d, J=47 Hz), 5.14 (1H, ddd, J=10, 10, 6 Hz), 5.93 (1H, s), 6.36 (1H, m), 6.81 (2x1H, d, J=8.5 Hz), 7.00 (1H, dt, J=16, 7 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.18 (1H, d, J=10 Hz), 7.49 (1H, d, J=10 Hz);

MASS (ES-) m/e 557;

[α]<sub>D</sub><sup>30</sup> = -108.6° (c=0.16, CHCl<sub>3</sub>).

35 Example 146

Compound E146 was obtained in a manner similar to Example 4.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7 Hz), 1.23-1.42 (4H, m), 1.28 (3H, s), 1.53-1.90 (6H, m), 2.07-2.24 (2H, m), 2.25-2.45 (2H, m), 2.54 (2H, m), 2.89 (1H, dd, J=13.5, 6.5 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.77 (3H, s), 3.85 (1H, m), 4.19 (1H, dt, J=10.5, 7.5 Hz), 4.67 (1H, m), 4.79 (2H, d, J=48 Hz), 5.13 (1H, ddd, J=10, 9.5, 6.5 Hz), 5.80 (1H, s), 6.81 (2x1H, d, J=8.5 Hz), 7.10 (1H, d, J=10.5 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.53 (1H, d, J=10 Hz);

MASS (ES-) m/e 559;

[α]<sub>D</sub><sup>30</sup> = -118.8° (c=0.40, CHCl<sub>3</sub>).

10 Example 147

To a stirred solution of the starting compound E146 (55 mg) in ethanol (4 ml) was added a solution of sodium borohydride in ethanol at 0°C and stirred at ambient temperature for half an hour. The reaction was quenched with water and most of the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate and washed with brine. The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using 50% ethyl acetate/hexane (v/v) as an eluting solvent mixture to give an amorphous, which was dissolved in tert-butyl alcohol and lyophilized to give Compound E147 (49 mg).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.53 (8H, m), 1.28 (3H, s), 1.56-1.90 (4H, m), 2.07-2.24 (3H, m), 2.25-2.40 (2H, m), 2.89 (1H, dd, J=14, 6 Hz), 3.18 (1H, dd, J=14, 9.5 Hz), 3.26 (1H, m), 3.77 (3H, s), 3.80-3.94 (2H, m), 4.20 (1H, m), 4.27 (1H, m), 4.41 (1H, ddd, J=47, 9.5, 3 Hz), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 9.5, 6 Hz), 5.94 (1H, d, J=5 Hz), 6.81 (2x1H, d, J=8.5 Hz), 7.11 (1H, d, J=10 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.54 (1H, d, J=10 Hz);

MASS (ES-): m/e 561;

30 [α]<sub>D</sub><sup>24</sup> = -107.5° (c=0.21, CHCl<sub>3</sub>).

Example 148

To a stirred solution of Compound E138 (165 mg) in dichloromethane (5 ml) was added a solution of diethylaminosulfurtrifluoride (71.7 mg) in dichloromethane at ambient temperature. The reaction mixture was stirred at the same temperature for three days. The solvent was removed under reduced pressure and

the residue was dissolved in ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution, water and brine. The organic layer was dried over sodium sulfate, filtered and evaporated under reduced pressure. The crude product was purified by preparative thin layer chromatography using 50% ethyl acetate/hexane (v/v) as a solvent mixture to give the Compound E148 (136 mg) as a white amorphous solid.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.84 (3H, t,  $J=7.3$  Hz), 0.88 (3H, d,  $J=6.5$  Hz), 1.22-1.44 (4H, m), 1.29 (3H, s), 1.47 (3H, dd,  $J=24$ , 7 Hz), 1.52-1.68 (3H, m), 1.82 (1H, m), 2.14 (1H, dq,  $J=14$ , 7.3 Hz), 2.26-2.43 (2H, m), 2.56-2.68 (3H, m), 2.72 (1H, dd,  $J=9.5$ , 8 Hz), 2.96 (1H, dd,  $J=13.5$ , 6 Hz), 3.24 (1H, dd,  $J=13.5$ , 10 Hz), 4.06 (1H, dd,  $J=9.5$ , 7 Hz), 4.20 (1H, dt,  $J=10$ , 7.5 Hz), 4.67 (1H, dd,  $J=8$ , 2 Hz), 4.86 (1H, dq,  $J=50$ , 7 Hz), 5.16 (1H, ddd,  $J=10$ , 10, 6 Hz), 5.84 (1H, s), 7.16 (1H, d,  $J=10$  Hz), 7.16-7.31 (5H, m), 7.54 (1H, d,  $J=10$  Hz);

MASS (ES-):  $m/e$  557;

$[\alpha]_D^{25} = -100.4^\circ$  ( $c=0.26$ ,  $\text{CHCl}_3$ ).

#### Example 149

To a stirred solution of the Compound E142 (99 mg) in tetrahydrofuran (4 ml) was added *n*-butyllithium (1.50 M in hexane, 0.60 ml) dropwise at  $-78^\circ\text{C}$ . The mixture was stirred at the same temperature for twenty-five minutes. The reaction mixture was quenched with water at the same temperature and the resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine, dried over sodium sulfate, filtered and evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using 50% ethyl acetate/hexane (v/v) as a solvent mixture to give Compound E149 (38 mg) as a white amorphous solid.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.80-0.96 (9H, m), 1.20-1.44 (6H, m), 1.29 (3H, s), 1.48-1.69 (5H, m), 1.81 (1H, m), 2.16 (1H, m), 2.26-2.42 (5H, m), 2.63 (1H, m), 2.72 (1H, m), 2.96 (1H, m), 3.25 (1H, m), 4.06 (1H, m), 4.19 (1H, m), 4.67 (1H, brd,  $J=8$  Hz), 5.16 (1H, m), 5.79 (1H, s), 7.14 (1H, d,  $J=10$  Hz), 7.18-7.32 (5H, m), 7.54 (1H, d,  $J=10$  Hz);

MASS (ES+):  $m/e$  569;

$[\alpha]_D^{21} = -116.2^\circ$  ( $c=0.18$ ,  $\text{CHCl}_3$ ).

#### Example 150

Compound E150 was obtained from the Compound (297) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 1.09 (9H, s), 1.23 (3H, d, J=7.0 Hz), 1.29 (3H, s), 1.36-1.92 (8H, m), 2.08-2.41 (4H, m),  
5 3.01 (1H, dd, J=13.6, 6.2 Hz), 3.22-3.33 (1H, m), 3.31 (1H, dd, J=13.6, 9.9 Hz), 3.83-3.92 (1H, m), 4.16-4.31 (1H, m), 4.27 (1H, q, J=7.0 Hz), 4.63-4.70 (1H, m), 5.23 (1H, ddd, J=10.6, 9.9, 6.2 Hz), 5.87 (1H, s), 6.62 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 6.6 Hz), 7.14 (1H, d, J=10.3 Hz), 7.19-7.25 (1H, m), 7.31-7.49 (8H, m), 7.54-7.78 (7H, m),  
10 7.90 (2H, d, J=8.1 Hz), 8.65-8.69 (1H, m);  
MASS (ES<sup>+</sup>): m/e 856.53 (M+1).

Example 151

Compound E151 was obtained from the Compound E150 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 1.11 (9H, s), 1.23 (3H, d, J=7.0 Hz), 1.29 (3H, s), 1.36-1.89 (8H, m), 2.10-2.26 (2H, m), 2.26-2.40 (2H, m), 2.47-2.56 (2H, m), 2.96-3.06 (1H, m), 3.23-3.37 (2H, m), 3.81-3.94 (1H, m), 4.09-4.31 (2H, m), 4.64-4.71 (1H, m), 5.17-5.30 (1H, m), 5.87 (1H, s), 7.08 (1H, d, J=10.3 Hz), 7.25-7.34 (1H, m),  
20 7.34-7.51 (8H, m), 7.58-7.88 (7H, m), 7.89-7.99 (2H, m), 8.67-8.77 (1H, m);  
MASS (ES<sup>+</sup>): m/e 858.45 (M+1).

Example 152

Compound E152 was obtained from the Compound E151 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 1.18-1.42 (2H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.47-1.90 (8H, m), 2.06-2.59 (6H, m), 3.01 (1H, dd, J=13.6, 9.5 Hz), 3.21-3.34 (1H, m), 3.31 (1H, dd, J=13.6, 5.5 Hz), 3.56 (1H, d, J=4.4 Hz), 3.81-3.93 (1H, m), 4.15-4.29 (2H, m), 4.62-4.71 (1H, m), 5.23 (1H, ddd, J=10.6, 9.5, 5.5 Hz), 5.88 (1H, s), 7.11 (1H, d, J=9.9 Hz), 7.18-7.25 (1H, m), 7.35 (2H, d, J=8.4 Hz), 7.59 (1H, d, J=10.6 Hz), 7.66-7.79 (2H, m), 7.90 (2H, d, J=8.4 Hz), 8.64-8.71 (1H, m);  
MASS (ES<sup>-</sup>): m/e 618.20 (M-1).

35 Example 153

Compound E153 was obtained from the Compound (300) in a manner

similar to Example 1.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.11 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.30 (3H, s), 1.37-1.92 (8H, m), 2.08-2.40 (4H, m), 3.06 (1H, dd, J=13.9, 6.6 Hz), 3.27-3.39 (1H, m), 3.30 (1H, dd, J=13.9, 9.2 Hz), 3.85-3.95 (1H, m), 4.18-4.32 (1H, m), 4.26 (1H, q, J=7.0 Hz), 4.67-4.73 (1H, m), 5.18-5.29 (1H, m), 5.93 (1H, s), 6.63 (1H, d, J=15.4 Hz), 6.88 (1H, dt, J=15.4, 6.6 Hz), 7.11 (1H, d, J=10.3 Hz), 7.32-7.52 (8H, m), 7.50 (2H, dd, J=4.4, 1.8 Hz), 7.55-7.70 (7H, m), 8.65 (2H, dd, J=4.4, 1.8 Hz);
- 10 MASS (ES<sup>+</sup>): m/e 856.38 (M+1).

Example 154

Compound E154 was obtained from the Compound E153 in a manner similar to Example 3.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t), 1.11 (9H, s), 1.20 (3H, d, J=7.0 Hz), 1.30 (3H, s), 1.36-1.90 (10H, m), 2.12-2.40 (4H, m), 2.48-2.56 (1H, m), 3.00-3.10 (1H, m), 3.24-3.39 (1H, m), 3.83-3.94 (1H, m), 4.13-4.29 (1H, m), 4.20 (1H, q, J=7.0 Hz), 4.67-4.73 (1H, m), 5.19-5.29 (1H, m), 5.92 (1H, s), 7.06 (1H, d, J=9.9 Hz), 7.33-7.53 (10H, m), 7.54-7.76 (7H, m), 8.62-8.68 (2H, m);
- 20 MASS (ES<sup>+</sup>): m/e 858.39 (M+1).

Example 155

Compound E155 was obtained from the Compound E154 in a manner similar to Example 6.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.17-1.43 (2H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.46-2.58 (12H, m), 3.04 (1H, dd, J=13.9, 6.6 Hz), 3.26-3.42 (1H, m), 3.29 (1H, dd, J=13.9, 9.2 Hz), 3.62 (1H, brs), 3.80-3.94 (1H, m), 4.14-4.30 (2H, m), 4.62-4.74 (1H, m), 5.23 (1H, ddd, J=10.3, 9.2, 6.6 Hz), 5.97 (1H, s), 7.08 (1H, d, J=10.3 Hz), 7.36 (2H, d, J=8.1 Hz), 7.45-7.53 (2H, m), 7.57 (2H, d, J=8.1 Hz), 7.64 (1H, d, J=10.3 Hz), 8.60-8.68 (2H, m);
- 30 MASS (ES<sup>+</sup>): m/e 620.20 (M+1).

Example 156

Compound E156 was obtained from the Compound (305) in a manner similar to Example 1.

- <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.29 (3H, s), 1.35-1.70 (6H, m), 1.72-1.89 (2H, m),

2.06-2.37 (4H, m), 2.58 (2H, t, J=7.6 Hz), 2.88-2.96 (2H, m), 2.95 (1H, dd, J=13.6, 6.2 Hz), 3.20 (1H, dd, J=13.6, 9.9 Hz), 3.25-3.38 (3H, m), 3.47-3.54 (2H, m), 3.56-3.66 (4H, m), 3.83-3.92 (1H, m), 4.17-4.27 (1H, m), 4.27 (1H, q, J=7.0 Hz), 5.17 (1H, ddd, J=9.9, 9.9, 6.2 Hz), 5.89 (1H, s), 6.61 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 6.6 Hz), 7.07-7.19 (1H, m), 7.11 (2H, d, J=8.4 Hz), 7.16 (2H, d, J=8.4 Hz), 7.31-7.47 (6H, m), 7.54 (1H, d, J=10.3 Hz), 7.59 (1H, d, J=8.1 Hz), 7.59 (1H, d, J=7.7 Hz), 7.65 (1H, d, J=8.1 Hz), 7.65 (1H, d, J=7.7 Hz);  
MASS (ES+): m/e 920.48 (M+1).

10 Example 157

Compound E157 was obtained from the Compound E156 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.17-1.32 (2H, m), 1.18 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.38-1.90 (8H, m), 2.04-2.20 (4H, m), 2.46-2.54 (2H, m), 2.58 (2H, t, J=8.7 Hz), 2.88-3.00 (1H, m), 2.93 (2H, t, J=8.7 Hz), 3.21 (1H, dd, J=14.1, 9.0 Hz), 3.28-3.38 (3H, m), 3.48-3.56 (2H, m), 3.61 (4H, s), 3.78-3.96 (1H, m), 4.10-4.27 (2H, m), 4.62-4.70 (1H, m), 5.10-5.22 (1H, m), 5.86 (1H, s), 7.06 (1H, d, J=9.9 Hz), 7.08-7.18 (4H, m), 7.32-7.51 (6H, m), 7.52-7.78 (5H, m);  
MASS (ES+): m/e 922.45 (M+1).

Example 158

Compound E158 was obtained from the Compound E157 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.19-1.41 (2H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.52-1.89 (8H, m), 2.06-2.40 (4H, m), 2.46 (2H, dt, J=11.7, 7.3 Hz), 2.58 (2H, t, J=7.7 Hz), 2.88-2.96 (2H, m), 2.95 (1H, dd, J=13.6, 6.2 Hz), 3.20 (1H, dd, J=13.6, 9.5 Hz), 3.24-3.40 (3H, m), 3.43-3.54 (2H, m), 3.54-3.67 (4H, m), 3.87 (1H, dt, J=8.1, 4.8 Hz), 4.14-4.29 (2H, m), 4.64-4.72 (1H, m), 5.17 (1H, ddd, J=10.6, 9.5, 6.2 Hz), 5.92 (1H, s), 7.05-7.19 (5H, m), 7.56 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 684.54 (M+1).

Example 159

35 Compound E159 was obtained from the Compound (308) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.25 (3H, d, J=7.0 Hz), 1.28 (12H, s), 1.38-1.61 (6H, m), 1.71-1.88 (2H, m), 2.09-2.38 (4H, m), 2.34 (2H, t, J=7.3 Hz), 2.89 (2H, t, J=7.3 Hz), 2.93 (1H, dd, J=13.5, 6.2 Hz), 3.21 (1H, dd, J=13.5, 9.2 Hz), 3.25-3.37 (1H, m), 3.83-3.91 (1H, m), 4.16-4.25 (1H, m), 4.28 (1H, q, J=7.0 Hz), 4.64-4.69 (1H, m), 5.07-5.19 (2H, m), 5.87 (1H, s), 6.61 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 6.6 Hz), 7.07-7.17 (5H, m), 7.31-7.49 (6H, m), 7.53 (1H, d, J=9.9 Hz), 7.57-7.68 (4H, m);  
MASS (ES<sup>+</sup>): m/e 906.30 (M+1).

10 Example 160

Compound E160 was obtained from the Compound E159 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.15-1.34 (2H, m), 1.25 (2H, d, J=7.0 Hz), 1.28 (12H, s), 1.39-1.88 (8H, m), 15 2.09-2.39 (4H, m), 2.35 (2H, t, J=7.7 Hz), 2.47-2.61 (2H, m), 2.89 (2H, t, J=7.7 Hz), 2.92 (1H, dd, J=13.9, 6.6 Hz), 3.20 (1H, dd, J=13.9, 9.9 Hz), 3.23-3.38 (1H, m), 3.81-3.91 (1H, m), 4.12-4.30 (2H, m), 4.64-4.70 (1H, m), 5.10 (1H, s), 5.16 (1H, ddd, J=10.3, 9.9, 6.6 Hz), 5.85 (1H, s), 7.07-7.18 (5H, m), 7.07 (1H, d, J=10.3 Hz), 7.33-7.49 (6H, m), 20 7.57 (1H, d, J=9.9 Hz), 7.59-7.68 (4H, m);  
MASS (ES<sup>+</sup>): m/e 908.49 (M+1).

Example 161

Compound E161 was obtained from the Compound E160 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.14-1.40 (2H, m), 1.28 (9H, s), 1.38 (3H, d, J=7.0 Hz), 1.45-1.70 (6H, m), 1.71-1.88 (2H, m), 2.07-2.41 (4H, m), 2.34 (2H, t, J=7.7 Hz), 2.46 (2H, dt, J=11.7, 7.3 Hz), 2.88 (2H, t, J=7.7 Hz), 2.92 (1H, dd, J=13.9, 5.9 Hz), 3.20 (1H, dd, J=13.9, 9.5 Hz), 3.22-3.33 (1H, m), 3.55 (1H, d, J=4.4 Hz), 30 3.80-3.92 (1H, m), 4.14-4.29 (2H, m), 4.65-4.71 (1H, m), 5.10 (1H, s), 5.16 (1H, ddd, J=10.3, 9.5, 5.9 Hz), 5.89 (1H, s), 7.09 (2H, d, J=8.1 Hz), 7.09-7.16 (1H, m), 7.14 (2H, d, J=8.1 Hz), 7.55 (1H, d, J=10.3 Hz);  
MASS (ES<sup>+</sup>): m/e 670.53 (M+1).

35 Example 162

To a solution of the Compound E138 (500 mg) in pyridine (1.2

ml) was added benzyl chloride (0.109 ml) under ice-cooling and the mixture was stirred for 5 hours under ambient temperature. To the reaction mixture was added an additional benzyl chloride (0.2 equivalent per Compound E138) and the mixture was stirred for 2 hours. To the mixture was added ice-cooled 1N hydrochloric acid. The mixture was stirred for 10 min, extracted with ethyl acetate, and the extract was washed with water, saturated aqueous sodium bicarbonate solution, water and saturated brine, and dried over sodium sulfate. The obtained crude compound was purified by column chromatography (eluting with hexane/ethyl acetate = 2/1 then 1/1) to give the objective Compound E162. Since the obtained Compound E162 included small amount of pyridine, the compound was dissolved into ethyl acetate, washed with 1N hydrochloric acid twice, then washed with saturated aqueous sodium bicarbonate solution, water and saturated brine, and dried over sodium sulfate. The mixture was filtered and the filtrate was evaporated to give purified Compound E162.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=7.3$  Hz), 0.88 (3H, d,  $J=6.6$  Hz), 1.22–1.42 (4H, m), 1.48–1.88 (4H, m), 1.53 (3H, d,  $J=7.0$  Hz), 2.07–2.21 (2H, m), 2.24–2.77 (7H, m), 2.95 (1H, dd,  $J=13.6$ , 5.9 Hz), 3.24 (1H, dd,  $J=13.6$ , 9.9 Hz), 4.05 (2H, dd,  $J=9.5$ , 7.3 Hz), 4.20 (1H, dt,  $J=10.3$ , 7.3 Hz), 4.67 (1H, dd,  $J=8.1$ , 2.2 Hz), 5.16 (1H, ddd,  $J=10.3$ , 9.9, 5.9 Hz), 5.33 (1H, q,  $J=7.0$  Hz), 5.87 (1H, s), 7.15 (1H, d,  $J=10.3$  Hz), 7.19–7.31 (5H, m), 7.44–7.51 (2H, m), 7.56 (1H, d,  $J=10.3$  Hz), 7.56–7.63 (1H, m), 8.08 (2H, d,  $J=8.4$  Hz);  
MASS (ES<sup>+</sup>):  $m/e$  661.51 ( $M+1$ ).

#### Example 163

Compound E163 was obtained from the Compound E162 in a manner similar to Preparation 307.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.85 (3H, t,  $J=7.3$  Hz), 1.04 (3H, d,  $J=7.0$  Hz), 1.16–1.40 (4H, m), 1.41–1.85 (4H, m), 1.52 (3H, d,  $J=7.0$  Hz), 1.96–2.12 (1H, m), 2.27–2.79 (8H, m), 3.10–3.23 (2H, m), 4.13 (2H, dd,  $J=9.9$ , 7.7 Hz), 4.21 (1H, dt,  $J=10.3$ , 7.3 Hz), 4.69–4.77 (1H, m), 5.17–5.29 (1H, m), 5.32 (1H, q,  $J=7.0$  Hz), 6.03 (1H, s), 7.09 (1H, d,  $J=10.6$  Hz), 7.43–7.51 (2H, m), 7.56–7.63 (1H, m), 7.63 (1H, d,  $J=10.3$  Hz), 8.08 (2H, d,  $J=8.4$  Hz);  
MASS (ES<sup>-</sup>):  $m/e$  627.53 ( $M-1$ ).

Example 164

Compound E164 was obtained from the Compound E163 in a manner similar to Preparation 308.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.3 Hz), 0.88 (3H, t, J=7.0 Hz), 1.06 (3H, d, J=6.6 Hz), 1.18-1.86 (12H, m), 1.28 (3H, s), 1.52 (3H, d, J=7.0 Hz), 1.97-2.12 (1H, m), 2.26-2.79 (8H, m), 2.98 (1H, dd, J=15.4, 11.0 Hz), 3.13-3.29 (4H, m), 4.16-4.27 (1H, m), 4.21 (1H, dt, J=10.3, 7.7 Hz), 4.72 (1H, d, J=7.7 Hz), 5.28-5.39 (1H, m), 5.32 (1H, q, J=7.0 Hz), 5.47-5.56 (1H, m), 5.88 (1H, s), 7.13 (1H, d, J=10.3 Hz), 7.39-7.53 (3H, m), 7.56-7.64 (1H, m), 8.08 (2H, d, J=7.7 Hz);  
MASS (ES<sup>+</sup>): m/e 698.56 (M+1).

Example 165

Compound E165 was obtained from the Compound E164 in a manner similar to Preparation 77.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 0.88 (3H, t, J=7.0 Hz), 1.07 (3H, d, J=6.6 Hz), 1.18-1.68 (10H, m), 1.30 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.72-1.85 (1H, m), 1.98-2.13 (1H, m), 2.28-2.55 (8H, m), 2.64-2.79 (1H, m), 2.99 (1H, dd, J=14.7, 11.0 Hz), 3.15-3.28 (3H, m), 3.45-3.56 (1H, m), 4.13-4.28 (3H, m), 4.73 (1H, d, J=7.7 Hz), 5.34 (1H, ddd, J=11.0, 9.9, 4.4 Hz), 5.45-5.53 (1H, m), 5.87 (1H, s), 7.16 (1H, d, J=10.3 Hz), 7.40 (1H, d, J=9.9 Hz);  
MASS (ES<sup>+</sup>): m/e 594.57 (M+1).

Example 166

Compound E166 was obtained from the Compound (312) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 1.09 (9H, s), 1.22 (3H, d, J=6.6 Hz), 1.31 (3H, s), 1.37-2.42 (12H, m), 2.71 (1H, dd, J=15.4, 4.8 Hz), 3.20 (1H, dd, J=15.4, 10.6 Hz), 3.74-3.87 (1H, m), 3.87-3.98 (1H, m), 4.18-4.31 (1H, m), 4.27 (1H, q, J=6.6 Hz), 4.68-4.74 (1H, m), 5.44 (1H, ddd, J=11.0, 10.6, 4.8 Hz), 5.97 (1H, s), 6.61 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 6.6 Hz), 7.05-7.15 (2H, m), 7.22-7.53 (10H, m), 7.49 (1H, d, J=10.6 Hz), 7.56-7.75 (5H, m);  
MASS (ES<sup>+</sup>): m/e 822.46 (M+1).

Example 167

Compound E167 was obtained from the Compound E166 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.13-1.35 (4H, m), 1.18 (3H, d, J=6.6 Hz), 1.31 (3H, s), 1.38-2.45 (8H, m), 2.46-2.55 (2H, m), 2.72 (1H, dd, J=15.8, 4.4 Hz), 3.21 (1H, dd, J=15.8, 11.0 Hz), 3.76-3.87 (1H, m), 3.87-3.99 (1H, m), 4.07-4.27 (1H, m),  
5 4.19 (1H, q, J=6.6 Hz), 4.67-4.74 (1H, m), 5.45 (1H, ddd, J=11.0, 10.6, 4.4 Hz), 5.96 (1H, s), 7.04 (1H, d, J=10.3 Hz), 7.09 (1H, dd, J=7.7, 7.3 Hz), 7.25-7.51 (10H, m), 7.54 (1H, d, J=10.6 Hz), 7.59-7.67 (4H, m), 7.70-7.75 (1H, m);  
MASS (ES<sup>+</sup>): m/e 824.55 (M+1).

10 Example 168

Compound E168 was obtained from the Compound E167 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.86 (3H, t, J=7.3 Hz), 1.15-1.44 (4H, m), 1.31 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.46-2.57 (12H, m), 2.72 (1H, dd, J=15.4, 4.4 Hz), 3.20 (1H, dd, J=15.4, 11.0 Hz), 3.56 (1H, d, J=4.8 Hz), 3.81 (1H, dt, J=10.3, 7.7 Hz), 3.87-3.98 (1H, m), 4.16-4.28 (2H, m), 4.68-4.75 (1H, m), 5.44 (1H, ddd, J=11.0, 10.3, 4.4 Hz), 5.97 (1H, s), 7.03-7.15 (1H, m), 7.07 (1H, d, J=9.9 Hz), 7.24-7.35 (2H, m), 7.37-7.47 (3H, m), 7.51 (1H, d, J=10.3 Hz);  
20 MASS (ES<sup>+</sup>): m/e 586.30 (M+1).

Example 169

Compound E169 was obtained from the Compound (315) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.28 (3H, s), 1.29 (3H, d, J=7.0 Hz), 1.38-1.92 (8H, m), 2.09-2.39 (4H, m), 2.95 (1H, dd, J=13.9, 6.6 Hz), 3.21 (1H, dd, J=13.9, 9.2 Hz), 3.22-3.35 (1H, m), 3.80-3.92 (1H, m), 4.15-4.33 (1H, m), 4.28 (1H, q, J=7.0 Hz), 4.59 (2H, s), 4.64-4.72 (1H, m), 5.15 (1H, ddd, J=10.3, 9.2, 6.6 Hz), 5.88 (1H, s), 6.62 (1H, d, J=15.8 Hz), 6.85 (1H, dt, J=15.8, 7.0 Hz), 6.92 (2H, d, J=8.8 Hz), 7.11 (1H, d, J=10.3 Hz), 7.16 (1H, dd, J=7.7, 7.7 Hz), 7.22 (2H, d, J=8.8 Hz), 7.30-7.50 (8H, m), 7.51-7.70 (7H, m), 8.25 (1H, brs);  
30 MASS (ES<sup>+</sup>): m/e 928.43 (M+1).

Example 170

35 Compound E170 was obtained from the Compound E169 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.15-1.33 (2H, m), 1.25 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.37-1.86 (8H, m), 2.10-2.38 (4H, m), 2.47-2.54 (2H, m), 2.93 (1H, dd, J=13.9, 6.2 Hz), 3.18-3.33 (1H, m), 3.20 (1H, dd, J=13.9, 9.2 Hz), 3.80-3.90 (1H, m),  
5 4.12-4.30 (2H, m), 4.58 (2H, s), 4.65-4.71 (1H, m), 5.14 (1H, ddd, J=10.3, 9.2, 6.2 Hz), 5.88 (1H, s), 6.91 (2H, d, J=8.4 Hz), 7.05 (1H, d, J=9.9 Hz), 7.16 (1H, dd, J=7.3, 7.3 Hz), 7.21 (2H, d, J=8.4 Hz), 7.32-7.51 (8H, m), 7.54-7.71 (7H, m), 8.24 (1H, brs);  
MASS (ES<sup>+</sup>): m/e 930.41 (M+1).

10 Example 171

Compound E171 was obtained from the Compound E170 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.22-1.41 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.49-1.89 (6H, m), 2.08-2.58  
15 (6H, m), 2.93 (1H, dd, J=13.6, 6.2 Hz), 3.19 (1H, dd, J=13.6, 9.2 Hz), 3.22-3.33 (1H, m), 3.55 (1H, d, J=4.8 Hz), 3.81-3.91 (1H, m), 4.14-4.28 (2H, m), 4.58 (2H, s), 4.65-4.71 (1H, m), 5.15 (1H, ddd, J=10.3, 9.2, 6.2 Hz), 5.88 (1H, s), 6.91 (2H, d, J=8.8 Hz), 7.08 (1H, d, J=10.3 Hz), 7.16 (1H, dd, J=7.3, 7.3 Hz), 7.21 (2H, d, J=8.8 Hz), 7.36  
20 (2H, dd, J=7.3, 7.3 Hz), 7.56 (1H, d, J=10.3 Hz), 7.57 (2H, d, J=7.3 Hz), 8.24 (1H, brs);  
MASS (ES<sup>+</sup>): m/e 692.37 (M+1).

Example 172

25 Compound E172 was obtained from the Compound (318) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 0.89 (3H, t, J=7.0 Hz), 1.09 (9H, s), 1.15-1.38 (4H, m), 1.22 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.38-1.91 (8H, m), 2.09-2.38 (4H, m), 2.87-2.96 (1H, dd, J=13.6, 6.2 Hz), 3.18 (1H, dd, J=13.6, 9.5 Hz), 3.21-3.37 (3H, m), 3.81-3.91  
30 (1H, m), 4.16-4.28 (1H, m), 4.27 (1H, q, J=7.0 Hz), 4.45 (2H, s), 4.64-4.71 (1H, m), 5.13 (1H, ddd, J=10.3, 9.5, 6.2 Hz), 5.91 (1H, s), 6.55 (1H, br), 6.61 (1H, d, J=15.8 Hz), 6.83 (2H, d, J=8.8 Hz), 6.86 (1H, dt, J=15.8, 6.6 Hz), 7.12 (1H, d, J=10.3 Hz), 7.18 (2H, d, J=8.8 Hz), 7.31-7.47 (6H, m), 7.55 (1H, d, J=10.3 Hz), 7.56-7.62 (2H, m),  
35 7.62-7.68 (2H, m);  
MASS (ES<sup>+</sup>): m/e 922.52 (M+1).

Example 173

Compound E173 was obtained from the Compound E172 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 0.89 (3H, t, J=7.0 Hz), 1.00-1.89 (14H, m), 1.10 (9H, s), 1.19 (3H, d, J=6.6 Hz), 1.28 (3H, s), 2.08-2.39 (4H, m), 2.46-2.56 (2H, m), 2.91 (1H, dd, J=13.6, 6.2 Hz), 3.18 (1H, dd, J=13.6, 9.5 Hz), 3.20-3.38 (3H, m), 3.79-3.91 (1H, m), 4.12-4.24 (1H, m), 4.18 (1H, q, J=7.0 Hz), 4.44 (2H, s), 4.64-4.70 (1H, m), 5.13 (1H, ddd, J=9.9, 9.5, 6.2 Hz), 5.88 (1H, s), 6.55 (1H, br), 6.83 (2H, d, J=8.8 Hz), 7.05 (1H, d, J=9.9 Hz), 7.18 (2H, d, J=8.8 Hz), 7.33-7.48 (6H, m), 7.58 (1H, d, J=9.9 Hz), 7.58-7.69 (4H, m);

MASS (ES<sup>+</sup>): m/e 924.63 (M+1).

Example 174

Compound E174 was obtained from the Compound E173 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 0.89 (3H, t, J=6.9 Hz), 1.18-1.42 (6H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.44-1.89 (8H, m), 2.07-2.58 (6H, m), 2.92 (1H, dd, J=13.9, 6.6 Hz), 3.18 (1H, dd, J=13.9, 9.5 Hz), 3.20-3.38 (3H, m), 3.46-3.61 (1H, m), 3.80-3.91 (1H, m), 4.14-4.30 (1H, m), 4.44 (2H, s), 4.64-4.72 (1H, m), 5.13 (1H, ddd, J=10.3, 9.5, 6.6 Hz), 5.92 (1H, s), 6.56 (1H, br), 6.83 (2H, d, J=8.4 Hz), 7.09 (1H, d, J=10.3 Hz), 7.18 (2H, d, J=8.4 Hz), 7.57 (1H, d, J=10.3 Hz);

MASS (ES<sup>+</sup>): m/e 686.60 (M+1).

Example 175

Compound E175 was obtained from the Compound (321) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.22 (3H, d, J=6.6 Hz), 1.29 (3H, s), 1.38-1.69 (12H, m), 1.72-1.88 (2H, m), 2.11-2.37 (4H, m), 2.89 (1H, dd, J=13.5, 6.2 Hz), 3.18 (1H, dd, J=13.5, 10.2 Hz), 3.19-3.31 (1H, m), 3.41-3.50 (2H, m), 3.51-3.58 (2H, m), 3.81-3.91 (1H, m), 4.17-4.29 (1H, m), 4.27 (1H, q, J=6.6 Hz), 4.64 (1H, s), 4.64-4.69 (1H, m), 5.13 (1H, ddd, J=10.6, 10.2, 6.2 Hz), 5.86 (1H, s), 6.60 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 5.9 Hz), 7.14 (1H, d, J=10.3 Hz), 7.14 (2H, d, J=8.4 Hz), 7.31-7.47 (6H, m), 7.52 (1H, d,

J=10.6 Hz), 7.55-7.69 (4H, m);

MASS (ES+): m/e 920.64 (M+1).

Example 176

Compound E176 was obtained from the Compound E175 in a manner  
5 similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.16-  
1.33 (2H, m), 1.18 (3H, d, J=7.0 Hz), 1.29 (3H, s), 1.39-1.88 (14H, m),  
2.08-2.37 (4H, m), 2.47-2.55 (2H, m), 2.88 (1H, dd, J=13.5, 5.9 Hz),  
3.18 (1H, dd, J=13.5, 10.3 Hz), 3.21-3.31 (1H, m), 3.43-3.51 (2H, m),  
10 3.52-3.60 (2H, m), 3.80-3.90 (1H, m), 4.13-4.23 (1H, m), 4.19 (1H, q,  
J=7.0 Hz), 4.64 (2H, s), 4.64-4.70 (1H, m), 5.12 (1H, ddd, J=10.3, 9.9,  
5.9 Hz), 5.85 (1H, s), 6.85 (2H, d, J=8.8 Hz), 7.08 (1H, d, J=10.3 Hz),  
7.14 (2H, d, J=8.8 Hz), 7.33-7.49 (6H, m), 7.55 (1H, d, J=9.9 Hz),  
7.59-7.68 (4H, m);

15 MASS (ES+): m/e 922.50 (M+1).

Example 177

Compound E177 was obtained from the Compound E170 in a manner  
similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.17-1.40 (2H, m),  
20 1.28 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.44-1.68 (12H, m), 1.72-1.88  
(2H, m), 2.05-2.55 (6H, m), 2.88 (1H, dd, J=13.6, 6.6 Hz), 3.18 (1H,  
dd, J=13.6, 9.9 Hz), 3.20-3.32 (1H, m), 3.42-3.50 (2H, m), 3.51-3.60  
(2H, m), 3.80-3.90 (1H, m), 4.12-4.28 (1H, m), 4.64 (2H, s), 4.64-4.70  
(1H, m), 5.12 (1H, ddd, J=10.3, 9.9, 6.6 Hz), 5.84 (1H, s), 6.85 (2H,  
25 d, J=8.8 Hz), 7.10 (1H, d, J=10.3 Hz), 7.14 (2H, d, J=8.8 Hz), 7.53  
(1H, d, J=10.3 Hz);

MASS (ES+): m/e 684.40 (M+1).

Example 178

Compound E178 was obtained from the Compound (324) in a manner  
30 similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.21  
(3H, d, J=7.0 Hz), 1.30 (3H, s), 1.39-1.90 (8H, m), 2.11-2.39 (4H, m),  
3.03 (1H, dd, J=13.6, 9.5 Hz), 3.27-3.38 (1H, m), 3.29 (1H, dd, J=13.6,  
6.6 Hz), 3.85-3.94 (1H, m), 4.18-4.28 (1H, m), 4.28 (1H, q, J=7.0 Hz),  
35 4.67-4.72 (1H, m), 5.23 (1H, ddd, J=10.3, 9.5, 6.6 Hz), 5.91 (1H, s),  
6.62 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 7.0 Hz), 7.11 (1H, d,

J=10.3 Hz), 7.30-7.48 (9H, m), 7.51 (2H, d, J=8.4 Hz), 7.56-7.68 (5H, m), 7.85 (1H, ddd, J=8.1, 4.0, 2.2 Hz), 8.58 (1H, dd, J=4.8, 1.5 Hz), 8.82 (1H, d, J=2.2 Hz);

MASS (ES+): m/e 856.41 (M+1).

5 Example 179

Compound E179 was obtained from the Compound E178 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.16-1.33 (2H, m), 1.25 (3H, d, J=7.0 Hz), 1.29 (3H, s), 1.37-1.88 (8H, m),  
10 2.12-2.38 (4H, m), 2.48-2.55 (2H, m), 2.99-3.08 (1H, m), 3.24-3.37 (2H, m), 3.84-3.94 (1H, m), 4.15-4.23 (1H, m), 4.26 (1H, q, J=7.0 Hz),  
4.67-4.72 (1H, m), 5.16-5.28 (1H, m), 5.90 (1H, s), 7.06 (1H, d, J=10.3 Hz), 7.32-7.48 (9H, m), 7.51 (2H, d, J=8.4 Hz), 7.58-7.67 (5H, m), 7.85 (1H, ddd, J=8.1, 4.8, 2.2 Hz), 8.57 (1H, dd, J=4.8, 1.5 Hz),  
15 8.81-8.83 (1H, m);

MASS (ES+): m/e 858.48 (M+1).

Example 180

Compound E180 was obtained from the Compound E179 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.19-1.42 (2H, m),  
20 1.29 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.53-1.92 (8H, m), 2.07-2.58 (6H, m), 3.04 (1H, dd, J=13.6, 6.2 Hz), 3.21-3.39 (1H, m), 3.29 (1H, dd, J=13.6, 9.2 Hz), 3.57 (1H, brs), 3.83-3.95 (1H, m), 4.15-4.29 (1H, m),  
4.67-4.74 (1H, m), 5.23 (1H, ddd, J=10.3, 9.2, 6.2 Hz), 5.95 (1H, s),  
25 7.10 (1H, d, J=10.3 Hz), 7.35 (2H, d, J=8.4 Hz), 7.36 (1H, d, J=8.1 Hz), 7.51 (1H, d, J=8.4 Hz), 7.62 (1H, d, J=10.3 Hz), 7.86 (1H, ddd, J=8.1, 4.0, 1.8 Hz), 8.58 (1H, d, J=4.0 Hz), 8.83 (1H, s);

MASS (ES+): m/e 620.48 (M+1).

Example 181

30 Compound E181 was obtained from the Compound (333) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.21 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.39-1.52 (2H, m), 1.54-1.72 (4H, m),  
1.74-1.92 (2H, m), 2.09-2.38 (4H, m), 2.93 (1H, dd, J=13.6, 6.2 Hz),  
35 3.17 (1H, dd, J=13.6, 9.2 Hz), 3.27-3.37 (1H, m), 3.81-3.90 (1H, m),  
4.17-4.29 (1H, m), 4.27 (1H, q, J=7.0 Hz), 4.66-4.71 (1H, m), 5.07-

5.17 (1H, m), 5.88 (1H, s), 6.61 (1H, d, J=15.7 Hz), 6.89 (1H, dt, J=15.7, 6.6 Hz), 7.04 (1H, d, J=10.6 Hz), 7.07 (1H, dd, J=8.4, 2.6 Hz), 7.30-7.49 (8H, m), 7.53-7.74 (5H, m);  
MASS (ES+): m/e 847.51 (M+1).

5 Example 182

Compound E182 was obtained from the Compound E181 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.15-1.33 (2H, m), 1.18 (3H, d, J=6.6 Hz), 1.28 (3H, s), 1.38-1.65 (4H, m),  
10 1.71-1.92 (2H, m), 2.09-2.39 (4H, m), 2.51 (2H, t, J=7.3 Hz), 2.93 (1H, dd, J=13.5, 6.6 Hz), 3.17 (1H, dd, J=13.5, 9.2 Hz), 3.27-3.38 (1H, m), 3.79-3.89 (1H, m), 4.14-4.25 (1H, m), 4.19 (1H, q, J=6.6 Hz), 4.65-4.72 (1H, m), 5.12 (1H, dd, J=9.9, 9.2, 6.6 Hz), 5.87 (1H, s), 6.98 (1H, d, J=9.9 Hz), 7.07 (1H, dd, J=8.4, 2.2 Hz), 7.32-7.49 (8H, m),  
15 7.58-7.69 (5H, m);  
MASS (ES+): m/e 849.53 (M+1).

Example 183

Compound E183 was obtained from the Compound E182 in a manner similar to Example 6.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.17-1.40 (2H, m), 1.28 (3H, s), 1.38 (2H, d, J=7.0 Hz), 1.52-1.72 (4H, m), 1.73-1.93 (2H, m), 2.07-2.57 (6H, m), 2.93 (1H, dd, J=13.9, 6.6 Hz), 3.17 (1H, dd, J=13.9, 9.2 Hz), 3.26-3.37 (1H, m), 3.55 (1H, d, J=4.4 Hz), 3.78-3.89 (1H, m), 4.13-4.29 (2H, m), 4.64-4.72 (1H, m), 5.06-5.17 (1H, m), 5.88  
25 (1H, s), 7.01 (1H, d, J=10.3 Hz), 7.07 (1H, dd, J=8.1, 2.2 Hz), 7.33 (1H, d, J=2.2 Hz), 7.35 (1H, d, J=8.1 Hz), 7.60 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 611.35 (M+1).

Example 184

30 Compound E184 was obtained from the Compound (341) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.23 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.38-1.94 (6H, m), 2.05-2.37 (4H, m), 3.00-3.10 (1H, m), 3.50 (1H, dd, J=14.3, 6.6 Hz), 3.64 (1H, dd, J=14.3, 9.2 Hz), 3.70-3.80 (1H, m), 4.17-4.29 (1H, m), 4.27 (1H, q, J=6.6 Hz),  
35 4.62-4.69 (1H, m), 5.43 (1H, ddd, J=9.9, 9.2, 6.6 Hz), 5.82 (1H, s), 6.62 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 6.6 Hz), 7.14 (1H, d,

J=10.3 Hz), 7.31-7.52 (9H, m), 7.53-7.69 (6H, m), 7.69-7.77 (1H, m), 7.85 (1H, d, J=8.4 Hz), 8.12 (1H, d, J=8.4 Hz);  
MASS (ES+): m/e 829.28 (M+1).

Example 185

5 Compound E185 was obtained from the Compound E185 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.78 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.14-1.33 (2H, m), 1.19 (3H, d, J=6.6 Hz), 1.27 (3H, s), 1.38-1.87 (8H, m), 2.06-2.21 (2H, m), 2.23-2.36 (2H, m), 2.52 (2H, t, J=7.7 Hz), 3.01-3.11 (1H, m), 3.50 (1H, dd, J=14.3, 6.6 Hz), 3.64 (1H, dd, J=14.3, 8.8 Hz), 3.70-3.79 (1H, m), 4.14-4.27 (1H, m), 4.19 (1H, q, J=6.6 Hz), 4.64-4.69 (1H, m), 5.38-5.48 (1H, m), 5.82 (1H, s), 7.09 (1H, d, J=11.0 Hz), 7.34-7.53 (9H, m), 7.53-7.78 (7H, m), 7.85 (1H, d, J=8.8 Hz), 8.13 (1H, d, J=8.8 Hz);  
15 MASS (ES+): m/e 831.29 (M+1).

Example 186

Compound E186 was obtained from the Compound E185 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.79 (3H, t, J=7.3 Hz), 1.19-1.41 (2H, m), 20 1.28 (3H, s), 1.39 (3H, d, J=7.0 Hz), 1.55-1.76 (7H, m), 1.76-1.91 (1H, m), 2.04-2.22 (2H, m), 2.23-2.40 (2H, m), 2.41-2.58 (2H, m), 3.05 (1H, dt, J=10.3, 7.3 Hz), 3.50 (1H, dd, J=14.2, 6.6 Hz), 3.56 (1H, d, J=4.4 Hz), 3.64 (1H, dd, J=14.3, 9.2 Hz), 3.69-3.79 (1H, m), 4.15-4.29 (1H, m), 4.23 (1H, q, J=7.0 Hz), 4.63-4.70 (1H, m), 5.43 (1H, ddd, J=10.3, 25 9.2, 6.6 Hz), 5.86 (1H, s), 7.12 (1H, d, J=10.3 Hz), 7.36-7.40 (2H, m), 7.49 (1H, ddd, J=8.1, 7.0, 1.1 Hz), 7.57 (1H, ddd, J=8.1, 6.6, 1.5 Hz), 7.66 (1H, d, J=10.3 Hz), 7.70-7.77 (1H, m), 7.85 (1H, dd, J=8.1, 1.5 Hz), 8.12 (1H, d, J=8.1 Hz);  
MASS (ES+): m/e 593.35 (M+1).

30 Example 187

Compound E187 was obtained from the Compound (347) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.35-1.92 (14H, m), 2.09-2.39 (4H, m), 35 2.98 (1H, dd, J=13.2, 5.5 Hz), 3.18-3.42 (4H, m), 3.58-3.77 (2H, m), 3.79-3.93 (1H, m), 4.15-4.27 (1H, m), 4.28 (1H, q, J=7.0 Hz), 4.66 (1H,

brd, J=5.9 Hz), 5.12-5.27 (1H, m), 5.91 (1H, s), 6.61 (1H, d, J=15.8 Hz), 6.86 (1H, dt, J=15.8, 6.6 Hz), 7.10 (1H, d, J=10.3 Hz), 7.22-7.49 (11H, m), 7.53-7.73 (4H, m);  
MASS (ES+): m/e 890.48 (M+1).

5 Example 188

Compound E188 was obtained from the Compound E187 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.15-1.33 (6H, m), 1.19 (3H, d, J=6.6 Hz), 1.29 (3H, s), 1.38-1.92 (10H, m),  
10 2.06-2.41 (4H, m), 2.47-2.56 (2H, m), 2.98 (1H, dd, J=13.2, 5.5 Hz),  
3.21-3.40 (4H, m), 3.59-3.77 (2H, m), 3.80-3.92 (1H, m), 4.10-4.26 (2H, m), 4.66 (1H, brd, J=5.9 Hz), 5.19 (1H, dt, J=9.5, 6.2 Hz), 5.91 (1H, s), 7.04 (1H, d, J=10.3 Hz), 7.22-7.49 (10H, m), 7.57-7.70 (5H, m);  
MASS (ES+): m/e 892.42 (M+1).

15 Example 189

Compound E189 was obtained from the Compound E188 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.20-1.93 (16H, m),  
1.29 (3H, s), 1.38 (3H, d, J=7.3 Hz), 2.06-2.60 (6H, m), 2.98 (1H, dd,  
20 J=13.2, 5.9 Hz), 3.19-3.42 (4H, m), 3.56 (1H, brd, J=4.0 Hz), 3.59-3.77 (2H, m), 3.80-3.92 (1H, m), 4.14-4.30 (2H, m), 4.66 (1H, brd, J=6.2 Hz), 5.19 (1H, dt, J=9.9, 6.2 Hz), 5.97 (1H, s), 7.08 (1H, d, J=10.3 Hz), 7.23-7.35 (4H, m), 7.60 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 654.57 (M+1).

25 Example 190

Compound E190 was obtained from the Compound (350) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.09 (9H, s), 1.23 (3H, d, J=6.6 Hz), 1.29 (3H, s), 1.37-1.93 (6H, m), 2.08-2.40 (6H, m),  
30 2.99-3.11 (1H, m), 3.23-3.37 (2H, m), 3.81-3.93 (1H, m), 4.17-4.33 (2H, m), 4.68 (1H, brd, J=6.6 Hz), 5.22 (1H, dt, J=9.5, 6.6 Hz), 5.92 (1H, s), 6.62 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 7.0 Hz), 7.02-7.50 (11H, m), 7.56-7.71 (8H, m), 7.74-7.84 (3H, m);  
MASS (ES+): m/e 898.39 (M+1).

35 Example 191

Compound E191 was obtained from the Compound E190 in a manner

similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.04-1.33 (4H, m), 1.10 (9H, s), 1.21 (3H, d, J=6.9 Hz), 1.29 (3H, s), 1.38-1.91 (6H, m), 2.03-2.41 (4H, m), 2.51 (2H, dt, J=7.0, 2.2 Hz), 2.99-3.12 (1H, m),  
5 3.22-3.36 (2H, m), 3.80-3.92 (1H, m), 4.14-4.31 (2H, m), 4.68 (1H, brd, J=5.9 Hz), 5.21 (1H, dt, J=9.5, 7.0 Hz), 5.95 (1H, s), 7.03 (1H, d, J=10.3 Hz), 7.15 (1H, t, J=7.3 Hz), 7.31-7.51 (9H, m), 7.57-7.72 (8H, m), 7.75-7.83 (3H, m);

MASS (ES<sup>+</sup>): m/e 900.47 (M+1).

10 Example 192

Compound E192 was obtained from the Compound E191 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.16-1.93 (10H, m), 1.29 (3H, s), 1.39 (3H, d, J=7.0 Hz), 2.04-2.59 (6H, m), 3.05 (1H, dd, J=13.6, 6.2 Hz), 3.23-3.37 (2H, m), 3.56 (1H, d, J=4.8 Hz), 3.80-3.89  
15 (1H, m), 4.15-4.30 (2H, m), 4.68 (1H, brd, J=7.0 Hz), 5.21 (1H, dt, J=10.3, 6.6 Hz), 5.96 (1H, s), 7.06 (1H, d, J=10.6 Hz), 7.15 (1H, t, J=7.3 Hz), 7.32-7.43 (4H, m), 7.57-7.68 (3H, m), 7.74-7.85 (3H, m);

MASS (ES<sup>+</sup>): m/e 662.53 (M+1).

20 Example 193

Compound E193 was obtained from the Compound (358) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.88 (3H, t, J=7.3 Hz), 0.91 (3H, d, J=6.6 Hz), 0.99 (3H, d, J=6.6 Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0 Hz),  
25 1.31 (3H, s), 1.37-1.71 (4H, m), 1.74-2.02 (3H, m), 2.11-2.44 (6H, m), 3.47-3.60 (1H, m), 3.83-3.96 (1H, m), 4.11-4.29 (1H, m), 4.48 (1H, t, J=10.6 Hz), 4.75 (1H, brd, J=6.3 Hz), 5.83 (1H, s), 6.61 (1H, d, J=15.5 Hz), 6.86 (1H, dt, J=15.5, 7.0 Hz), 7.17 (1H, d, J=10.3 Hz), 7.30-7.47 (7H, m), 7.56-7.69 (4H, m);

30 MASS (ES<sup>+</sup>): m/e 731.57 (M+1).

Example 194

Compound E194 was obtained from the Compound E193 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.88 (3H, t, J=7.3 Hz), 0.91 (3H, d, J=6.6 Hz), 0.98 (3H, d, J=6.6 Hz), 1.10 (9H, s), 1.15-1.65 (7H, m), 1.18 (3H, d, J=6.6 Hz), 1.30 (3H, s), 1.70-2.01 (4H, m), 2.11-2.44 (4H, m),  
35

2.46-2.54 (2H, m), 3.47-3.59 (1H, m), 3.81-3.96 (1H, m), 4.09-4.24 (2H, m), 4.47 (1H, t, J=10.3 Hz), 4.75 (1H, brd, J=7.3 Hz), 5.83 (1H, s), 7.10 (1H, d, J=10.3 Hz), 7.32-7.48 (7H, m), 7.56-7.67 (4H, m);

MASS (ES+): m/e 733.65 (M+1).

5 Example 195

Compound E195 was obtained from the Compound E194 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.88 (3H, t, J=7.4 Hz), 0.90 (3H, d, J=6.6 Hz), 0.99 (3H, d, J=7.0 Hz), 1.21-1.40 (4H, m), 1.30 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.52-1.70 (3H, m), 1.70-2.00 (3H, m), 2.12-2.58 (7H, m), 3.47-3.57 (1H, m), 3.56 (1H, d, J=4.4 Hz), 3.83-3.95 (1H, m), 4.13-4.29 (2H, m), 4.48 (1H, t, J=10.3 Hz), 4.75 (1H, dd, J=7.7, 1.8 Hz), 5.85 (1H, s), 7.14 (1H, d, J=10.3 Hz), 7.38 (1H, d, J=9.9 Hz);  
MASS (ES+): m/e 495.49 (M+1).

15 Example 196

Compound E196 was obtained from the Compound (367) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.7 Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.29 (3H, s), 1.37-1.93 (6H, m), 2.10-2.38 (6H, m), 2.94 (1H, dd, J=13.6, 6.2 Hz), 3.16-3.34 (2H, m), 3.80-3.92 (1H, m), 3.87 (3H, s), 4.17-4.32 (2H, m), 4.64-4.71 (1H, m), 5.17 (1H, dt, J=9.5, 5.9 Hz), 5.91 (1H, brs), 6.62 (1H, d, J=15.8 Hz), 6.77 (1H, dd, J=8.1, 1.8 Hz), 6.82 (1H, d, J=1.8 Hz), 6.88 (1H, dd, J=15.8, 6.6 Hz), 7.09 (1H, d, J=10.6 Hz), 7.25 (1H, d, J=8.1 Hz), 7.31-7.51 (6H, m), 7.54-7.69 (5H, m);  
MASS (ES+): m/e 843.39 (M+1).

Example 197

Compound E197 was obtained from the Compound E196 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.11 (9H, s), 1.15-1.35 (10H, m), 1.19 (3H, d, J=6.6 Hz), 1.29 (3H, s), 2.02-2.41 (4H, m), 2.45-2.57 (2H, m), 2.94 (1H, dd, J=13.5, 6.1 Hz), 3.22 (1H, dd, J=13.5, 9.5 Hz), 3.23-3.35 (1H, m), 3.79-3.92 (1H, m), 3.88 (3H, s), 4.10-4.28 (2H, m), 4.68 (1H, brd, J=6.2 Hz), 5.11-5.23 (1H, m), 5.89 (1H, brs), 6.78 (1H, dd, J=8.1, 1.8 Hz), 6.83 (1H, brs), 7.03 (1H, d, J=9.9 Hz), 7.26 (1H, d, J=8.1 Hz), 7.32-7.49 (6H, m), 7.58-7.69 (5H, m);

MASS (ES+): m/e 845.40 (M+1).

Example 198

Compound E198 was obtained from the Compound E197 in a manner similar to Example 6.

5  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.84 (3H, t,  $J=7.3$  Hz), 1.18-1.41 (7H, m),  
1.29 (3H, s), 1.38 (3H, d,  $J=7.0$  Hz), 1.70-1.92 (3H, m), 2.04-2.59 (6H,  
m), 2.93 (1H, dd,  $J=13.6$ , 6.6 Hz), 3.21 (1H, dd,  $J=13.6$ , 9.9 Hz),  
3.23-3.34 (1H, m), 3.55 (1H, d,  $J=4.8$  Hz), 3.79-3.92 (1H, m), 3.87 (3H,  
s), 4.13-4.30 (2H, m), 4.68 (1H, brd,  $J=5.9$  Hz), 5.16 (1H, dt,  $J=9.5$ ,  
10 5.5 Hz), 5.90 (1H, brs), 6.77 (1H, dd,  $J=8.1$ , 1.8 Hz), 6.81 (1H, brs),  
7.06 (1H, d,  $J=10.3$  Hz), 7.25 (1H, d,  $J=8.1$  Hz), 7.59 (1H, d,  $J=10.3$   
Hz);

MASS (ES+): m/e 607.27 (M+1).

Example 199

15 Compound E199 was obtained from the Compound (374) in a manner similar to Example 1.

$^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=7.3$  Hz), 1.09 (9H, s), 1.23  
(3H, d,  $J=6.6$  Hz), 1.29 (3H, s), 1.37-1.92 (6H, m), 2.09-2.41 (6H, m),  
2.97 (1H, dd,  $J=13.6$ , 6.2 Hz), 3.23 (1H, dd,  $J=13.6$ , 9.5 Hz), 3.25-  
20 3.36 (1H, m), 3.80-3.94 (1H, m), 4.16-4.32 (2H, m), 4.69 (1H, dd,  
 $J=8.1$ , 2.2 Hz), 5.16 (1H, dt,  $J=9.5$ , 6.6 Hz), 5.85 (1H, s), 6.62 (1H,  
d,  $J=15.8$  Hz), 6.80-6.98 (3H, m), 7.01 (1H, d,  $J=7.7$  Hz), 7.09 (1H, d,  
 $J=9.9$  Hz), 7.19-7.29 (1H, m), 7.31-7.47 (6H, m), 7.53-7.69 (5H, m);

MASS (ES+): m/e 797.30 (M+1).

25 Example 200

Compound E200 was obtained from the Compound E199 in a manner similar to Example 3.

$^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.83 (3H, t,  $J=7.3$  Hz), 0.99-1.91 (10H, m),  
1.10 (9H, s), 1.19 (3H, d,  $J=7.0$  Hz), 1.28 (3H, s), 2.06-2.40 (4H, m),  
30 2.45-2.55 (2H, m), 2.96 (1H, dd,  $J=13.6$ , 6.6 Hz), 3.23 (1H, dd,  $J=13.6$ ,  
9.2 Hz), 3.25-3.36 (1H, m), 3.79-3.91 (1H, m), 4.12-4.25 (2H, m), 4.68  
(1H, brd,  $J=8.0$  Hz), 5.16 (1H, dt,  $J=10.3$ , 6.2 Hz), 5.84 (1H, s),  
6.85-7.07 (4H, m), 7.19-7.29 (1H, m), 7.31-7.49 (6H, m), 7.55-7.68 (5H,  
m);

35 MASS (ES+): m/e 799.31 (M+1).

Example 201

Compound E201 was obtained from the Compound E200 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.20-1.41 (5H, m), 1.29 (3H, s), 1.38 (3H, d, J=7.0 Hz), 1.52-1.70 (2H, m), 1.71-1.91 (3H, m), 2.08-2.58 (6H, m), 2.97 (1H, dd, J=13.6, 6.2 Hz), 3.22 (1H, dd, J=13.6, 9.2 Hz), 3.26-3.36 (1H, m), 3.56 (1H, d, J=4.8 Hz), 3.81-3.91 (1H, m), 4.15-4.29 (2H, m), 4.69 (1H, dd, J=7.7, 2.2 Hz), 5.16 (1H, dt, J=9.6, 6.6 Hz), 5.86 (1H, s), 6.86-6.98 (2H, m), 7.01 (1H, d, J=7.7 Hz), 7.06 (1H, d, J=10.3 Hz), 7.19-7.30 (1H, m), 7.58 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 561.36 (M+1).

#### Example 202

Compound E202 was obtained in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.12 (9H, s), 1.28 (3H, s), 1.31-1.64 (5H, m), 1.68-1.87 (2H, m), 2.07-2.39 (5H, m), 2.96 (1H, dd, J=13.6, 6.6 Hz), 3.18-3.32 (2H, m), 3.80-3.93 (1H, m), 4.12-4.24 (1H, m), 4.66 (1H, brd, J=7.3 Hz), 5.13-5.24 (1H, m), 5.16 (1H, s), 5.78 (1H, s), 6.54 (1H, d, J=15.8 Hz), 6.76 (1H, dt, J=15.8, 6.6 Hz), 7.10 (1H, d, J=10.3 Hz), 7.19-7.57 (19H, m), 7.59-7.66 (2H, m);

MASS (ES+): m/e 841.20 (M+1).

#### Example 203

Compound E203 was obtained from the Compound E202 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 0.93-1.35 (6H, m), 1.13 (9H, s), 1.27 (3H, s), 1.38-1.54 (1H, m), 1.60-1.86 (3H, m), 2.07-2.47 (6H, m), 2.96 (1H, dd, J=13.6, 6.6 Hz), 3.18-3.33 (2H, m), 3.79-3.90 (1H, m), 4.05-4.16 (1H, m), 4.65 (1H, brd, J=8.1 Hz), 5.09 (1H, s), 5.12-5.23 (1H, m), 5.78 (1H, s), 7.02 (1H, d, J=10.3 Hz), 7.15-7.48 (18H, m), 7.55 (1H, d, J=10.3 Hz), 7.62-7.68 (2H, m);

MASS (ES+): m/e 843.19 (M+1).

#### Example 204

Compound E204 was obtained from Compound E203 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.0 Hz), 1.07-1.90 (10H, m), 1.27 (3H, s), 2.06-2.44 (6H, m), 2.96 (1H, dd, J=13.6, 5.9 Hz), 3.17-3.33 (2H, m), 3.79-3.91 (1H, m), 4.08-4.21 (1H, m), 4.66 (1H, brd,

J=7.0 Hz), 5.07 (1H, s), 5.11-5.24 (1H, m), 5.85 (1H, s), 7.08 (1H, d, J=10.3 Hz), 7.16-7.66 (11H, m);  
MASS (ES+): m/e 605.36 (M+1).

#### Example 205

5       The Compound E138 (147 mg) was reacted with benzyl 2,2,2-trichloroacetimidate (200 mg) in dichloromethane (3 ml) in the presence of the catalytic amount of trifluoromethanol (7.93 mg) under ice-cooling for 1 hour. The temperature of the reaction mixture was raised to ambient temperature and the mixture was stirred for 16 hours.  
10      The reaction was quenched with saturated aqueous sodium bicarbonate solution (2 ml) under ice-cooling. The reaction mixture was extracted with ethyl acetate, washed with saturated aqueous sodium bicarbonate solution (20 ml x 2) and saturated brine (20 ml), and dried over sodium sulfate. The crude product was purified by reverse phase  
15      preparative chromatography and lyophilized from t-butanol to give the objective Compound E205.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.7 Hz), 0.88 (3H, d, J=6.6 Hz), 1.21-1.90 (9H, m), 1.28 (3H, s), 1.33 (3H, d, J=7.0 Hz), 2.07-2.43 (3H, m), 2.43-2.71 (3H, m), 2.73 (1H, t, J=8.1 Hz), 2.95 (1H, dd, J=13.6, 5.9 Hz), 3.24 (1H, dd, J=13.6, 9.5 Hz), 3.92 (1H, q, J=7.0 Hz), 4.06 (1H, dd, J=9.5, 7.3 Hz), 4.19 (1H, dt, J=10.3, 7.7 Hz), 4.49 (1H, d, J=11.7 Hz), 4.55 (1H, d, J=11.7 Hz), 4.67 (1H, dd, J=8.1, 2.2 Hz), 5.16 (1H, dt, J=10.3, 5.9 Hz), 5.79 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.17-7.41 (10H, m), 7.54 (1H, d, J=10.3 Hz);  
20      MASS (ES+): m/e 647.39 (M+1).

#### Example 206

      The Compound E138 (190.7 mg) was reacted with 3,4-dihydro-2H-pyran (86.4 mg) in dichloromethane (3 ml) in the presence of pyridinium p-toluenesulfonate under ambient temperature for 20 hours.  
30      The reaction was quenched with saturated aqueous sodium bicarbonate solution (2 ml). The reaction mixture was extracted with ethyl acetate (50 ml), washed with saturated aqueous sodium bicarbonate solution (20 ml x 2) and saturated brine (20 ml), and dried over sodium sulfate. The mixture was purified by preparative thin layer  
35      chromatography (eluting with ethyl acetate/hexane=2/1) and lyophilized from t-butanol to give the objective Compound E206.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.7 Hz), 0.88 (3H, d, J=6.6 Hz), 1.24-1.95 (15H, m), 1.28 (3H, s), 1.36 (3H, d, J=7.0 Hz), 2.07-2.23 (1H, m), 2.25-2.77 (6H, m), 2.95 (1H, dd, J=13.6, 5.9 Hz), 3.24 (1H, dd, J=13.6, 9.5 Hz), 3.38-3.56 (1H, m), 3.77-3.93 (1H, m), 4.02-4.13 (1H, m), 4.13-4.25 (1H, m), 4.28 (1H, q, J=7.0 Hz), 4.56 (0.5H, dd, J=4.4, 2.9 Hz), 4.61 (0.5H, dd, J=5.1, 2.9 Hz), 4.67 (1H, dd, J=8.1, 1.8 Hz), 5.16 (1H, dt, J=10.3, 6.2 Hz), 5.80 (1H, s), 7.10-7.32 (6H, m), 7.51-7.59 (1H, m);  
MASS (ES+): m/e 557.39 (M+1).

10 Example 207

The Compound E138 (100 mg) was mixed with (2-methoxyethoxy)methyl chloride (44.8 mg) in dichloromethane (2 ml) in the presence of ethyldiisopropylamine (0.156 ml) and the catalytic amount of tetrabutylammonium iodide, and the mixture was refluxed at 15 100°C for 36 hours. The reaction mixture was cooled to the ambient temperature and the solvent was removed by evaporation. The residue was extracted with ethyl acetate, and the extract was washed with 1N hydrochloric acid, saturated aqueous sodium bicarbonate and saturated brine and dried over sodium sulfate. The mixture was purified by 20 flush chromatography and lyophilized from ethyl acetate to give the objective Compound E207.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 0.88 (3H, d, J=6.2 Hz), 1.22-1.90 (8H, m), 1.28 (3H, s), 1.32 (3H, d, J=7.0 Hz), 2.08-2.78 (8H, m), 2.95 (1H, dd, J=13.6, 5.9 Hz), 3.24 (1H, dd, J=13.6, 9.9 Hz), 3.39 (3H, s), 3.50-3.60 (2H, m), 3.68-3.76 (2H, m), 4.01-4.25 (3H, m), 4.67 (1H, dd, J=8.4, 2.6 Hz), 4.73 (1H, d, J=7.0 Hz), 4.79 (1H, d, J=7.0 Hz), 5.10-5.22 (1H, m), 5.82 (1H, s), 7.15 (1H, d, J=10.3 Hz), 7.18-7.33 (5H, m), 7.55 (1H, d, J=10.3 Hz);  
MASS (ES-): m/e 643.36(M-1).

30 Example 208

Compound E208 was obtained from the Compound (386) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=6.5 Hz), 1.29 (3H, s), 1.38-1.52 (2H, m), 1.56-1.93 (4H, m), 2.02-2.42 (6H, m), 3.01 (1H, dd, J=13.5, 6.5 Hz), 3.22 (1H, dd, J=13.5, 9 Hz), 3.34 (1H, m), 3.86 (1H, m), 4.23 (1H, m), 4.27 (1H, q,

J=6.5 Hz), 4.68 (1H, brd, J=8 Hz), 5.22 (1H, m), 5.83 (1H, s), 6.63 (1H, d, J=15.5 Hz), 6.87 (1H, dt, J=15.5, 7 Hz), 7.02 (1H, d, J=10 Hz), 7.17 (2x1H, brd, J=5.5 Hz), 7.31-7.49 (6H, m), 7.56-7.72 (5H, m), 8.51 (2x1H, brd, J=5.5 Hz);

5 MASS (ES+): m/e 780.29.

Example 209

Compound E209 was obtained from the Compound E208 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 1.10 (3x3H, s),  
10 1.16-1.34 (4H, m), 1.18 (3H, d, J=6.5 Hz), 1.28 (3H, s), 1.38-1.68 (3H, m), 1.72-1.92 (3H, m), 2.02-2.40 (4H, m), 2.51 (2H, m), 3.01 (1H, dd, J=13.5, 6.5 Hz), 3.21 (1H, dd, J=13.5, 9 Hz), 3.34 (1H, m), 3.85 (1H, m), 4.13-4.26 (2H, m), 4.68 (1H, brd, J=8 Hz), 5.21 (1H, m), 5.84 (1H, s), 6.96 (1H, d, J=10 Hz), 7.17 (2x1H, d, J=6 Hz), 7.32-7.49 (6H, m),  
15 7.57-7.72 (5H, m), 8.51 (2x1H, d, J=6 Hz);

MASS (ES+): m/e 782.38.

Example 210

Compound E210 was obtained from the Compound E209 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.20-1.45 (4H, m),  
20 1.29 (3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.92 (6H, m), 2.06-2.56 (6H, m), 3.01 (1H, dd, J=13.5, 7 Hz), 3.21 (1H, dd, J=13.5, 8.5 Hz), 3.34 (1H, m), 3.56 (1H, br), 3.86 (1H, m), 4.15-4.30 (2H, m), 4.69 (1H, brd, J=8 Hz), 5.21 (1H, ddd, J=10.5, 8.5, 7 Hz), 5.85 (1H, s), 6.99 (1H, d, J=10 Hz), 7.17 (2x1H, d, J=6 Hz), 7.63 (1H, d, J=10.5 Hz), 8.51 (2x1H, d, J=6 Hz);

MASS (ES+): m/e 543.38;

[α]<sub>D</sub><sup>22</sup> = -113.7° (c=0.20, CHCl<sub>3</sub>).

Example 211

30 Compound E211 was obtained from the Compound (390) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.09 (3x3H, s),  
1.22 (3H, d, J=7 Hz), 1.38-1.51 (3H, m), 1.56-1.91 (4H, m), 2.08-2.40 (6H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz),  
35 3.26 (1H, m), 3.86 (1H, m), 4.21 (1H, dt, J=10.5, 7.7 Hz), 4.27 (1H, q, J=7 Hz), 4.50 (1H, ddd, J=5, 1.5, 1.5 Hz), 4.66 (1H, dd, J=8, 2 Hz),

5.13 (1H, ddd, J=10, 9.5, 6 Hz), 5.27 (1H, ddt, J=10.5, 1.5, 1.5 Hz),  
5.40 (1H, ddt, J=17.3, 1.5, 1.5 Hz), 5.79 (1H, s), 6.04 (1H, ddt,  
J=17.3, 10.5, 5 Hz), 6.62 (1H, brd, J=15, 7 Hz), 6.82 (2x1H, d, J=8.5  
Hz), 6.86 (1H, dt, J=15.7, 7 Hz), 7.13 (1H, d, J=10.5 Hz), 7.13 (2x1H,  
5 d, J=8.5 Hz), 7.30-7.48 (6H, m), 7.50 (1H, d, J=10 Hz), 7.56-7.69 (4H,  
m);  
MASS (ES-): m/e 836.08.

#### Example 212

Compound E212 was obtained from the Compound E211 in a manner  
10 similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.02 (3H, t, J=7.4  
Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=7 Hz), 1.21-1.32 (4H, m), 1.28 (3H,  
s), 1.38-1.64 (3H, m), 1.68-1.85 (5H, m), 2.07-2.40 (4H, m), 2.51 (2H,  
m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26  
15 (1H, m), 3.85 (1H, m), 3.88 (2H, t, J=6.6 Hz), 4.13-4.23 (2H, m), 4.66  
(1H, dd, J=8, 2.5 Hz), 5.13 (1H, ddd, J=10.2, 10, 6 Hz), 5.79 (1H, s),  
6.80 (2x1H, d, J=8.5 Hz), 7.08 (1H, d, J=10.3 Hz), 7.12 (2x1H, d,  
J=8.5 Hz), 7.33-7.48 (6H, m), 7.54 (1H, d, J=10.2 Hz), 7.58-7.67 (4H,  
m);  
20 MASS (ES+): m/e 839.32.

#### Example 213

Compound E213 was obtained from the Compound E212 in a manner  
similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.02 (3H, t, J=7.4  
25 Hz), 1.22-1.40 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.52-  
1.70 (3H, m), 1.71-1.90 (5H, m), 2.06-2.58 (6H, m), 2.88 (1H, dd,  
J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.55 (1H, d,  
J=4.7 Hz), 3.86 (1H, m), 3.87 (2H, t, J=6.6 Hz), 4.13-4.29 (2H, m),  
4.66 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.81 (1H, s), 6.80 (2x1H,  
30 d, J=8.5 Hz), 7.11 (1H, d, J=10 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.52  
(1H, d, J=10 Hz);  
MASS (ES+): m/e 601.44

$[\alpha]_D^{22} = -121.0^\circ$  (c=0.23, CHCl<sub>3</sub>).

#### Example 214

35 Compound E214 was obtained from the Compound (393) in a manner  
similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22 (3H, d, J=7 Hz), 1.29 (3H, s), 1.31 (2x3H, d, J=6 Hz), 1.38-1.53 (2H, m), 1.54-1.89 (4H, m), 2.08-2.39 (6H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.21 (1H, dt, J=10, 7.5 Hz), 4.27 (1H, q, J=7 Hz), 4.49 (1H, qq, J=6, 6 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.14 (1H, ddd, J=10, 9.5, 6 Hz), 5.80 (1H, s), 6.61 (1H, d, J=16 Hz), 6.79 (2x1H, d, J=8.5 Hz), 6.86 (1H, dt, J=16, 7 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.14 (1H, d, J=10 Hz), 7.30-7.47 (6H, m), 7.50 (1H, d, J=10 Hz), 7.55-7.68 (4H, m);

10 MASS (ES<sup>+</sup>): m/e 837.53.

#### Example 215

Compound E215 was obtained from the Compound E214 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=7 Hz), 1.20-1.33 (4H, m), 1.28 (3H, s), 1.31 (2x3H, d, J=6 Hz), 1.38-1.51 (2H, m), 1.55-1.62 (1H, m), 1.70-1.87 (3H, m), 2.08-2.24 (2H, m), 2.25-2.39 (2H, m), 2.51 (2H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7 Hz), 4.49 (1H, qq, J=6, 6 Hz), 4.66 (1H, dd, J=8, 2.5 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.80 (1H, s), 6.89 (2x1H, d, J=8.8 Hz), 7.08 (1H, d, J=10 Hz), 7.12 (2x1H, d, J=8.8 Hz), 7.33-7.48 (6H, m), 7.54 (1H, d, J=10 Hz), 7.58-7.68 (4H, m);

20 MASS (ES<sup>+</sup>): m/e 839.58.

#### Example 216

25 Compound E216 was obtained from the Compound E215 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.40 (4H, m), 1.28 (3H, s), 1.31 (2x3H, d, J=6 Hz), 1.38 (3H, d, J=7 Hz), 1.54-1.90 (6H, m), 2.08-2.58 (6H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.56 (1H, d, J=4.5 Hz), 3.86 (1H, m), 4.14-4.29 (2H, m), 4.49 (1H, qq, J=6, 6 Hz), 4.67 (1H, dd, J=8, 2 Hz), 5.13 (1H, ddd, J=10, 9.5, 6 Hz), 5.81 (1H, s), 6.79 (2x1H, d, J=8.7 Hz), 7.12 (1H, d, J=10 Hz), 7.12 (2x1H, d, J=8.7 Hz), 7.52 (1H, d, J=10 Hz);

30 MASS (ES<sup>+</sup>): m/e 601.39;

[α]<sub>D</sub><sup>23</sup> = -121.4° (c=0.25, CHCl<sub>3</sub>).

Example 217

Compound E217 was obtained from the Compound (397) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 0.96 (3H, t, J=7.3 Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=6.7 Hz), 1.28 (3H, s), 1.38-1.91 (10H, m), 2.08-2.40 (6H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.86 (1H, m), 3.92 (2H, t, J=6.5 Hz), 4.21 (1H, dt, J=10, 7.7 Hz), 4.27 (1H, q, J=6.7 Hz), 4.66 (1H, dd, J=8, 2.5 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.79 (1H, s), 6.61 (1H, d, J=15.8 Hz), 6.80 (2x1H, d, J=8.5 Hz), 6.86 (1H, dt, J=15.8, 7 Hz), 7.12 (2x1H, d, J=8.5 Hz), 7.31-7.47 (6H, m), 7.50 (1H, d, J=10 Hz), 7.56-7.69 (4H, m);

MASS (ES<sup>+</sup>): m/e 851.37.

Example 218

Compound E218 was obtained from the Compound E217 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 0.96 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=6.5 Hz), 1.20-1.32 (4H, m), 1.28 (3H, s), 1.39-1.62 (6H, m), 1.68-1.87 (4H, m), 2.08-2.40 (6H, m), 2.51 (2H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (1H, m), 3.92 (2H, t, J=6.5 Hz), 4.10-4.23 (2H, m), 4.66 (1H, dd, J=8, 2 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.80 (1H, s), 6.80 (2x1H, d, J=8.5 Hz), 7.08 (1H, d, J=10.5 Hz), 7.13 (2x1H, d, J=8.5 Hz), 7.33-7.48 (6H, m), 7.54 (1H, d, J=10 Hz), 7.58-7.68 (4H, m);

MASS (ES<sup>+</sup>): m/e 853.43.

Example 219

Compound E219 was obtained from the Compound E218 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 0.96 (3H, t, J=7.3 Hz), 1.21-1.89 (14H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.3 Hz), 2.07-2.57 (6H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.55 (1H, d, J=5 Hz), 3.86 (1H, m), 3.92 (2H, t, J=6.5 Hz), 4.13-4.29 (2H, m), 4.67 (1H, dd, J=8, 2 Hz), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.84 (1H, s), 6.80 (2x1H, d, J=8.3 Hz), 7.12 (2x1H, d, J=8.3 Hz), 7.12 (1H, d, J=10 Hz), 7.52 (1H, d, J=10 Hz);

MASS (ES+): m/e 615.44.

Example 220

Compound E220 was obtained from the Compound (406) in a manner similar to Example 1.

5  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.95 (3H, t,  $J=7.4$  Hz), 1.09 (3x3H, s),  
1.23 (3H, d,  $J=6.5$  Hz), 1.39–1.53 (2H, m), 1.58–1.90 (6H, m), 1.74 (3H,  
s), 2.10–2.38 (4H, m), 2.95 (1H, dd,  $J=13.5$ , 6 Hz), 3.20 (1H, m), 3.27  
(1H, dd,  $J=13.5$ , 10 Hz), 3.88 (1H, m), 4.22 (1H, m), 4.27 (1H, q,  
 $J=6.5$  Hz), 4.67 (1H, dd,  $J=8$ , 2 Hz), 5.16 (1H, ddd,  $J=10$ , 10, 6 Hz),  
10 5.85 (1H, s), 6.61 (1H, d,  $J=16$  Hz), 6.87 (1H, dt,  $J=16$ , 7 Hz), 7.15  
(1H, d,  $J=10$  Hz), 7.18–7.49 (12H, m), 7.56–7.69 (4H, m);

MASS (ES+): m/e 779.37.

Example 221

15 Compound E221 was obtained from the Compound E220 in a manner similar to Example 3.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.95 (3H, t,  $J=7.3$  Hz), 1.10 (3x3H, s),  
1.19 (3H, d,  $J=7$  Hz), 1.21–1.32 (4H, m), 1.40–1.52 (2H, m), 1.54–1.86  
(6H, m), 1.73 (3H, s), 2.17 (1H, m), 2.31 (1H, m), 2.51 (2H, m), 2.95  
(1H, dd,  $J=13.5$ , 5.5 Hz), 3.20 (1H, m), 3.28 (1H, dd,  $J=13.5$ , 10 Hz),  
20 3.87 (1H, m), 4.12–4.24 (2H, m), 4.65 (1H, dd,  $J=8$ , 2 Hz), 5.16 (1H,  
ddd,  $J=10$ , 10, 5.5 Hz), 5.86 (1H, s), 7.09 (1H, d,  $J=10$  Hz), 7.17–7.32  
(5H, m), 7.33–7.51 (7H, m), 7.58–7.68 (4H, m);

MASS (ES+): m/e 803.38.

Example 222

25 Compound E222 was obtained from the Compound E221 in a manner similar to Example 6.

$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ): 0.95 (3H, t,  $J=7.4$  Hz), 1.24–1.41 (4H, m),  
1.38 (3H, d,  $J=7$  Hz), 1.58–1.88 (8H, m), 1.73 (3H, s), 2.15 (1H, m),  
2.27–2.58 (3H, m), 2.95 (1H, dd,  $J=13.5$ , 5.5 Hz), 3.20 (1H, m), 3.27  
30 (1H, dd,  $J=13.5$ , 10 Hz), 3.55 (1H, d,  $J=4.7$  Hz), 3.86 (1H, m), 4.20  
(1H, dt,  $J=10$ , 7.5 Hz), 4.22 (1H, q,  $J=7$  Hz), 4.65 (1H, dd,  $J=8$ , 2 Hz),  
5.15 (1H, ddd,  $J=10$ , 10, 5.5 Hz), 5.86 (1H, s), 7.12 (1H, d,  $J=10$  Hz),  
7.17–7.32 (5H, m), 7.44 (1H, d,  $J=10$  Hz);

MASS (ES+): m/e 543.38;

35  $[\alpha]_D^{23} = -106.8^\circ$  ( $c=0.23$ ,  $\text{CHCl}_3$ ).

Example 223

Compound E223 was obtained from the Compound (409) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=6.6 Hz), 1.28 (3H, s), 1.38-1.51 (2H, m), 1.53-1.94 (12H, m), 2.08-2.39 (6H, m), 2.88 (1H, dd, J=13.5, 5.8 Hz), 3.17 (1H, dd, J=13.5, 9.9 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.21 (1H, dt, J=10.1, 7.7 Hz), 4.27 (1H, q, J=6.6 Hz), 4.63-4.74 (2H, m), 5.13 (1H, ddd, J=10.2, 9.9, 5.8 Hz), 5.83 (1H, s), 6.61 (1H, d, J=15.6 Hz), 6.78 (2x1H, d, J=8.8 Hz), 6.86 (1H, dt, J=15.6, 6.8 Hz), 7.11 (2x1H, d, J=8.8 Hz), 7.13 (1H, d, J=10.1 Hz), 7.31-7.48 (6H, m), 7.50 (1H, d, J=10.2 Hz), 7.56-7.69 (4H, m);

MASS (ES<sup>+</sup>): m/e 863.22.

#### Example 224

Compound E224 was obtained from the Compound E223 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.15-1.32 (4H, m), 1.18 (3H, d, J=6.7 Hz), 1.28 (3H, s), 1.39-1.67 (6H, m), 1.68-1.95 (8H, m), 2.08-2.40 (4H, m), 2.51 (2H, m), 2.88 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (1H, m), 4.13-4.24 (2H, m), 4.63-4.74 (2H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.82 (1H, s), 6.77 (2x1H, d, J=8.5 Hz), 7.08 (1H, d, J=10 Hz), 7.11 (2x1H, d, J=8.5 Hz), 7.32-7.48 (6H, m), 7.54 (1H, d, J=10 Hz), 7.58-7.69 (4H, m);

MASS (ES<sup>+</sup>): m/e 865.88.

#### Example 225

Compound E225 was obtained from the Compound E224 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.40 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.52-1.70 (6H, m), 1.71-1.95 (8H, m), 2.08-2.57 (6H, m), 2.87 (1H, dd, J=13.5, 6 Hz), 3.17 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.55 (1H, d, J=4.5 Hz), 3.86 (1H, m), 4.13-4.29 (2H, m), 4.63-4.74 (2H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.81 (1H, s), 6.77 (2x1H, d, J=8.7 Hz), 7.11 (2x1H, d, J=8.7 Hz), 7.12 (1H, d, J=10 Hz), 7.51 (1H, d, J=10 Hz);

MASS (ES<sup>+</sup>): m/e 627.10.

#### Example 226

Compound E226 was obtained from the Compound (412) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.22 (3H, d, J=6.5 Hz), 1.28 (3H, s), 1.38-1.52 (2H, m), 1.56-1.92 (4H, m), 2.08-2.39 (6H, m), 2.90 (1H, dd, J=14, 6 Hz), 3.18 (1H, dd, J=14, 9.5 Hz), 3.26 (1H, m), 3.80 (3H, s), 3.86 (1H, m), 4.15-4.31 (2H, m), 4.60 (2H, s), 4.67 (1H, dd, J=8, 2.5 Hz), 5.13 (1H, ddd, J=10, 9.5, 6 Hz), 5.83 (1H, s), 6.62 (1H, d, J=8.5 Hz), 6.85 (1H, m), 7.12 (1H, d, J=10 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.31-7.49 (6H, m), 7.52 (1H, d, J=10 Hz), 7.57-7.69 (4H, m);  
MASS (ES<sup>+</sup>): m/e 867.27.

Example 227

Compound E227 was obtained from the Compound E226 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.16-1.32 (4H, m), 1.18 (3H, d, J=6.6 Hz), 1.28 (3H, s), 1.40-1.51 (2H, m), 1.59 (1H, m), 1.69-1.87 (3H, m), 2.08-2.39 (4H, m), 2.51 (2H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.80 (3H, s), 3.85 (1H, m), 4.18 (1H, m), 4.25 (1H, q, J=6.6 Hz), 4.60 (2H, s), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.83 (1H, s), 6.81 (2x1H, d, J=8.8 Hz), 7.06 (1H, d, J=10 Hz), 7.15 (2x1H, d, J=10 Hz), 7.33-7.49 (6H, m), 7.55 (1H, d, J=10 Hz), 7.59-7.70 (4H, m);  
MASS (ES<sup>+</sup>): m/e 869.20.

Example 228

Compound E228 was obtained from the Compound E227 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.44 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.70 (3H, m), 1.72-1.90 (3H, m), 2.08-2.58 (6H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.57 (1H, d, J=4.5 Hz), 3.80 (3H, s), 3.85 (1H, m), 4.14-4.29 (2H, m), 4.60 (2H, s), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 9.5, 6 Hz), 5.86 (1H, s), 6.82 (2x1H, d, J=8.5 Hz), 7.10 (1H, d, J=10 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.53 (1H, d, J=10 Hz);  
MASS (ES<sup>+</sup>): m/e 631.39.

Example 229

The Compound E227 (155 mg) was hydrolyzed with 1N aqueous sodium

hydroxide (0.357 ml) in methanol (4 ml) under ambient temperature for 1 hour. The reaction mixture was neutralized with 1N hydrochloric acid and the solvent was removed by evaporation. The residue was partitioned between ethyl acetate and saturated brine, and the ethyl acetate layer was dried over sodium sulfate and evaporated. The residue was purified by thin layer chromatography (eluting with methanol/CHCl<sub>3</sub>=1/5) to give the objective Compound E229 as a white foam.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.4 Hz), 1.10 (3x3H, s), 1.14-1.32 (4H, m), 1.18 (3H, d, J=7 Hz), 1.27 (3H, s), 1.36-1.86 (6H, m), 2.02-2.56 (6H, m), 2.84 (1H, dd, J=13.5, 5.5 Hz), 3.08-3.28 (2H, m), 3.81 (1H, m), 4.17 (1H, m), 4.18 (1H, q, J=7 Hz), 4.54 (2H, s), 4.63 (1H, m), 5.10 (1H, m), 5.95 (1H, s), 6.80 (2x1H, d, J=8.5 Hz), 7.10 (2x1H, d, J=8.5 Hz), 7.15 (1H, d, J=10 Hz), 7.32-7.47 (6H, m), 7.55-7.67 (5H, m);

MASS (ES-): m/e 853.39.

#### Example 230

Compound E230 was obtained from the Compound E229 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.40 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.88 (6H, m), 2.06-2.57 (6H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.84 (1H, m), 4.19 (1H, m), 4.24 (1H, q, J=7 Hz), 4.60 (1H, s), 4.67 (1H, m), 5.12 (1H, ddd, J=10, 9.5, 6 Hz), 5.97 (1H, s), 6.84 (2x1H, d, J=8.5 Hz), 7.12 (1H, d, J=10 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.56 (1H, d, J=10 Hz);

MASS (ES-): m/e 615.46.

#### Example 231

Compound E231 was obtained from the Compound (415) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=7 Hz), 1.29 (3H, s), 1.38-1.51 (2H, m), 1.55-1.91 (4H, m), 2.08-2.39 (6H, m), 2.95 (1H, dd, J=13.5, 6 Hz), 3.23 (1H, dd, J=13.5, 10 Hz), 3.28 (1H, m), 3.87 (1H, m), 4.21 (1H, dt, J=10.2, 7.7 Hz), 4.27 (1H, q, J=7 Hz), 4.67 (1H, m), 5.18 (1H, ddd, J=10, 10, 6 Hz), 5.21 (1H, dd, J=11.8, 1 Hz), 5.71 (1H, dd, J=17.6, 1 Hz), 5.88

(1H, s), 6.62 (1H, d, J=15.8 Hz), 6.67 (1H, dd, J=17.6, 11.8 Hz), 6.87 (1H, dt, J=15.8, 7 Hz), 7.13 (1H, d, J=10.2 Hz), 7.19 (2x1H, d, J=8 Hz), 7.30-7.48 (8H, m), 7.55 (1H, d, J=10 Hz), 7.57-7.68 (4H, m);  
MASS (ES+): m/e 805.62.

5 Example 232

Compound E232 was obtained from the Compound E231 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.5 Hz), 1.10 (3x3H, s), 1.15-1.32 (4H, m), 1.18 (3H, d, J=7 Hz), 1.20 (3H, t, J=7.5 Hz), 1.28 (3H, s), 1.38-1.64 (3H, m), 1.70-1.87 (3H, m), 2.08-2.39 (4H, m), 2.51 (2H, m), 2.60 (2H, q, J=7.5 Hz), 2.92 (1H, dd, J=13.5, 6 Hz), 3.21 (1H, dd, J=13.5, 9.5 Hz), 3.28 (1H, m), 3.86 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7 Hz), 4.68 (1H, m), 5.17 (1H, ddd, J=10, 9.5, 6 Hz), 5.88 (1H, s), 7.09 (1H, d, J=10 Hz), 7.10 (2x1H, d, J=8.5 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.33-7.48 (6H, m), 7.56 (1H, d, J=10 Hz), 7.58-7.68 (4H, m);

MASS (ES+): m/e 809.60.

Example 233

20 Compound E233 was obtained from the Compound E232 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.20 (3H, t, J=7.7 Hz), 1.24-1.40 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.52-1.90 (6H, m), 2.08-2.55 (6H, m), 2.60 (2H, t, J=7.7 Hz), 2.93 (1H, dd, J=13.5, 6 Hz), 3.20 (1H, dd, J=13.5, 9.5 Hz), 3.28 (1H, m), 3.56 (1H, d, J=4.5 Hz), 3.87 (1H, m), 4.14-4.28 (2H, m), 4.68 (1H, dd, J=8, 2 Hz), 5.17 (1H, ddd, J=10, 9.5, 6 Hz), 5.90 (1H, s), 7.10 (2x1H, d, J=8.5 Hz), 7.12-7.17 (3H, m), 7.54 (1H, d, J=10 Hz);

MASS (ES+): m/e 571.58;

$[\alpha]_D^{25} = -119.3^\circ$  (c=0.24, CHCl<sub>3</sub>).

30 Example 234

Compound E234 was obtained from the Compound (418) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7 Hz), 1.09 (3x3H, s), 1.23 (3H, d, J=7 Hz), 1.28 (3H, s), 1.36-1.88 (6H, m), 2.08-2.38 (6H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7 Hz), 4.67 (1H, m), 5.13 (1H, m),

5.17 (2H, s), 5.88 (1H, s), 6.62 (1H, brd, J=16 Hz), 6.87 (1H, dt, J=16, 7 Hz), 6.90 (2x1H, d, J=8.7 Hz), 7.14 (1H, d, J=10 Hz), 7.14 (2x1H, d, J=8.7 Hz), 7.23 (1H, m), 7.30-7.75 (13H, m), 8.59 (1H, m);  
MASS (ES+): m/e 886.46.

5 Example 235

Compound E235 was obtained from the Compound E234 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.16-1.32 (4H, m), 1.18 (3H, d, J=7 Hz), 1.28 (3H, s), 1.38-1.88 (6H, m), 2.07-2.40 (4H, m), 2.51 (2H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.85 (1H, m), 4.12-4.24 (2H, m), 4.67 (1H, m), 5.13 (1H, ddd, J=10, 9.5, 6 Hz), 5.17 (2H, s), 5.83 (1H, s), 6.90 (2x1H, d, J=8.5 Hz), 7.08 (1H, d, J=10 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.22 (1H, dd, J=7.5, 5 Hz), 7.33-7.48 (6H, m), 7.50 (1H, d, J=7.5 Hz), 7.55 (1H, d, J=10 Hz), 7.59-7.67 (4H, m), 7.70 (1H, ddd, J=7.5, 7.5, 1.5 Hz), 8.59 (1H, brd, J=5 Hz);

MASS (ES+): m/e 888.43.

Example 236

20 Compound E236 was obtained from the Compound E235 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.20-1.42 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.52-1.90 (6H, m), 2.06-2.58 (6H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.57 (1H, br), 3.85 (1H, m), 4.13-4.29 (2H, m), 4.67 (1H, m), 5.13 (1H, m), 5.17 (2H, s), 5.93 (1H, s), 6.90 (2x1H, d, J=8.6 Hz), 7.12 (1H, d, J=10 Hz), 7.14 (2x1H, d, J=8.6 Hz), 7.23 (1H, m), 7.47-7.58 (2H, m), 7.71 (1H, dd, J=7.5, 7.5 Hz), 8.59 (1H, brd, J=4 Hz);

MASS (ES+): m/e 650.55;

[α]<sub>D</sub><sup>25</sup> = -89.0° (c=0.41, CHCl<sub>3</sub>).

30 Example 237

Compound E237 was obtained from the Compound (422) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.09 (3x3H, s), 1.23 (3H, d, J=6.6 Hz), 1.29 (3H, s), 1.38-1.52 (2H, m), 1.57-1.92 (4H, m), 2.08-2.41 (6H, m), 2.13 (3H, s), 2.96 (1H, dd, J=13.5, 6 Hz), 3.24 (1H, dd, J=13.5, 9.5 Hz), 3.30 (1H, m), 3.88 (1H, m), 4.22 (1H, m),

4.27 (1H, q, J=6.6 Hz), 4.68 (1H, m), 5.05 (1H, brs), 5.19 (1H, ddd, J=10.3, 9.5, 6 Hz), 5.35 (1H, s), 5.91 (1H, s), 6.62 (1H, d, J=16 Hz), 6.87 (1H, dt, J=16, 7 Hz), 7.14 (1H, d, J=10.5 Hz), 7.19 (2x1H, d, J=8 Hz), 7.31-7.48 (8H, m), 7.55 (1H, d, J=10.3 Hz), 7.55-7.70 (4H, m);

5 MASS (ES+): m/e 819.44.

Example 238

Compound E238 was obtained from the Compound E237 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.10 (3x3H, s),  
10 1.16-1.32 (4H, m), 1.18 (3H, d, J=6.6 Hz), 1.21 (2x3H, d, J=7 Hz),  
1.28 (3H, s), 1.38-1.65 (3H, m), 1.68-1.88 (3H, m), 2.08-2.40 (4H, m),  
2.51 (2H, m), 2.86 (1H, qq, J=7, 7 Hz), 2.93 (1H, dd, J=13.8, 6.3 Hz),  
3.21 (1H, dd, J=13.8, 9.5 Hz), 3.29 (1H, m), 3.86 (1H, m), 4.19 (1H,  
m), 4.19 (1H, q, J=6.6 Hz), 4.68 (1H, dd, J=8, 2 Hz), 5.18 (1H, ddd,  
15 J=10.3, 9.5, 6.3 Hz), 5.90 (1H, s), 7.05-7.18 (4H, m), 7.09 (1H, d,  
J=10.2 Hz), 7.33-7.48 (6H, m), 7.56 (1H, d, J=10.3 Hz), 7.59-7.67 (4H,  
m);

MASS (ES+): m/e 823.51.

Example 239

20 Compound E239 was obtained from the Compound E238 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.21 (2x3H, d, J=7  
Hz), 1.24-1.42 (4H, m), 1.54-1.90 (6H, m), 2.08-2.59 (6H, m), 2.85 (1H,  
qq, J=7, 7 Hz), 2.93 (1H, dd, J=14, 6 Hz), 3.20 (1H, dd, J=14, 10 Hz),  
25 3.55 (1H, d, J=5 Hz), 3.87 (1H, m), 4.14-4.29 (2H, m), 4.68 (1H, dd,  
J=8, 2 Hz), 5.18 (1H, ddd, J=10.3, 10, 6 Hz), 5.85 (1H, s), 7.05-7.20  
(5H, m), 7.53 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 585.46;

[α]<sub>D</sub><sup>25</sup> = -124.5° (c=0.27, CHCl<sub>3</sub>).

30 Example 240

Compound E240 was obtained from the Compound (426) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.08 (2x3H, s), 0.84 (3H, t, J=7.3 Hz),  
0.93 (3x3H, s), 1.09 (3x3H, s), 1.24 (3H, d, J=6.8 Hz), 1.29 (3H, s),  
35 1.38-1.51 (2H, m), 1.54-1.91 (4H, m), 2.08-2.40 (6H, m), 2.94 (1H, dd,  
J=13.5, 6 Hz), 3.23 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.86 (1H,

m), 4.21 (1H, dt, J=10.2, 7.7 Hz), 4.27 (1H, q, J=6.8 Hz), 4.66 (1H, dd, J=8, 2 Hz), 4.69 (1H, s), 5.18 (1H, ddd, J=10.2, 9.5, 6 Hz), 5.86 (1H, s), 6.62 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 7 Hz), 7.14 (1H, d, J=10.2 Hz), 7.19 (2x1H, d, J=8.5 Hz), 7.23 (2x1H, d, J=8.5 Hz),  
5 7.31-7.48 (6H, m), 7.53 (1H, d, J=10.2 Hz), 7.56-7.69 (4H, m);  
MASS (ES+): m/e 923.66.

#### Example 241

Compound E241 was obtained from the Compound E240 in a manner similar to Example 3.

10 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.19 (3H, d, J=6.6 Hz), 1.20-1.32 (4H, m), 1.28 (3H, s), 1.36-1.88 (6H, m), 2.07-2.40 (4H, m), 2.51 (2H, m), 2.96 (1H, dd, J=14, 6 Hz), 3.23 (1H, dd, J=14, 9.5 Hz), 3.28 (1H, m), 3.86 (1H, m), 4.12-4.25 (2H, m), 4.65 (2H, s), 4.67 (1H, m), 5.18 (1H, m), 5.92 (1H, s), 7.07 (1H, d, J=10.3 Hz), 7.23 (2x1H, d, J=8 Hz), 7.28 (2x1H, d, J=8 Hz), 7.33-7.49  
15 (6H, m), 7.56-7.70 (5H, m);  
MASS (ES+): m/e 811.55.

#### Example 242

20 Compound E242 was obtained from the Compound E241 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.42 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.90 (6H, m), 2.06-2.57 (6H, m), 2.96 (1H, dd, J=13.5, 6.2 Hz), 3.23 (1H, dd, J=13.5, 9.5 Hz), 3.28 (1H, m), 3.56 (1H, d, J=4.5 Hz), 3.86 (1H, m), 4.14-4.28 (2H, m), 4.66  
25 (2H, s), 4.68 (1H, m), 5.18 (1H, ddd, J=10.3, 9.5, 6.2 Hz), 5.92 (1H, s), 7.10 (1H, d, J=10 Hz), 7.23 (2x1H, d, J=8 Hz), 7.28 (2x1H, d, J=8 Hz), 7.57 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 573.57;  
[α]<sub>D</sub><sup>25</sup> = -117.8° (c=0.25, CHCl<sub>3</sub>).

#### Example 243

Compound E243 was obtained from the Compound (438) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.70-0.84 (6H, m), 0.96-1.96 (12H, m), 1.09 (3x3H, s), 1.24 (3H, d, J=7 Hz), 1.38 (3H, t, J=7 Hz), 2.23 (2H, m),  
35 2.46 (1H, m), 2.68 (1H, m), 2.80 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.97 (2H, q, J=7 Hz), 4.28 (1H, q, J=7 Hz), 4.42-4.63

(4H, m), 4.82 (1H, m), 5.81-5.94 (2H, br), 6.14 (1H, d, J=9.5 Hz), 6.61 (1H, d, J=16 Hz), 6.77 (2x1H, d, J=9 Hz), 6.85 (1H, dt, J=16, 7 Hz), 7.10 (2x1H, d, J=9 Hz), 7.30-7.48 (6H, m), 7.51-7.74 (4H, m);  
MASS (ES+): m/e 851.54.

5 Example 244

Compound E244 was obtained from the Compound E243 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.74 (3H, m), 0.79 (3H, d, J=7 Hz), 1.04-1.96 (16H, m), 1.10 (3x3H, s), 1.18 (3H, d, J=7 Hz), 1.38 (3H, d, J=7 Hz), 2.41-2.55 (3H, m), 2.71 (1H, m), 2.80 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.97 (1H, q, J=7 Hz), 4.18 (1H, q, J=7 Hz), 4.41-4.63 (4H, m), 4.83 (1H, m), 5.80-5.98 (2H, m), 6.17 (1H, d, J=11 Hz), 6.76 (2x1H, d, J=8.5 Hz), 7.09 (2x1H, d, J=8.5 Hz), 7.33-7.48 (6H, m), 7.58-7.68 (4H, m);

15 MASS (ES+): m/e 853.57.

Example 245

Compound E245 was obtained from the Compound E244 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.68-0.80 (6H, m), 0.79 (3H, d, J=6.5 Hz), 1.11 (1H, m), 1.21-1.98 (15H, m), 1.38 (3H, d, J=7 Hz), 1.39 (3H, t, J=7 Hz), 2.34-2.58 (3H, m), 2.71 (1H, m), 2.80 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.56 (1H, d, J=5 Hz), 3.97 (2H, q, J=7 Hz), 4.23 (1H, m), 4.42-4.63 (4H, m), 4.84 (1H, m), 5.93-6.05 (2H, m), 6.20 (1H, d, J=10.5 Hz), 6.76 (2x1H, d, J=8.5 Hz), 7.09 (2x1H, d, J=8.5 Hz);

25 MASS (ES+): m/e 615.62;

$[\alpha]_D^{25} = -117.8^\circ$  (c=0.20, CHCl<sub>3</sub>).

Example 246

30 Compound E246 was obtained from the Compound (444) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.23 (3H, d, J=7 Hz), 1.28 (3H, d, J=7 Hz), 1.40-1.53 (2H, m), 1.61-1.91 (4H, m), 2.12-2.38 (4H, m), 2.93 (1H, dd J=14, 6 Hz), 3.16 (1H, dt, J=10, 7 Hz), 3.22 (1H, dd, J=14, 10 Hz), 3.91 (1H, dt, J=10, 4 Hz), 4.23-4.35 (1H, m), 4.327 (1H, q, J=7 Hz), 4.51-4.68 (2H, m), 5.12 (1H, dt, J=6, 10 Hz), 6.10 (1H, d, J=10 Hz), 6.53 (1H, d, J=10 Hz), 6.61 (1H, d, J=15 Hz), 6.87 (1H, dt,

J=15, 8 Hz), 7.14-7.48 (12H, m), 7.57-7.70 (4H, m);

MASS: m/z 751.28 (M+H)<sup>+</sup>.

Example 247

Compound E247 was obtained from the Compound E246 in a manner  
5 similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.15-1.35 (2H, m), 1.18 (3H, d, J=7 Hz), 1.28 (3H, d, J=7 Hz), 1.37-1.50 (2H, m), 1.55-1.90 (6H, m), 2.14-2.41 (2H, m), 2.51 (2H, t, J=7 Hz), 2.93 (1H, dd J=14, 6 Hz), 3.17 (1H, dt, J=10, 7 Hz), 3.22 (1H, dd, J=14, 10 Hz), 3.90 (1H, dt, J=10, 4 Hz), 4.18 (1H, q, J=7 Hz), 4.25 (1H, J=10, 7 Hz), 4.52-4.68 (2H, m), 5.12 (1H, dt, J=6, 10 Hz), 6.09 (1H, d, J=10 Hz), 6.55 (1H, d, J=10 Hz), 7.11 (1H, d J=10 Hz), 7.18-7.33 (5H, m), 7.33-7.50 (6H, m), 7.59-7.74 (4H, m).

Example 248

15 Compound E248 was obtained from the Compound E247 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.22-1.42 (4H, m), 1.28 (3H, d, J=7 Hz), 1.38 (3H, d, J=7 Hz), 1.53-1.91 (6H, m), 2.10-2.59 (2H, m), 2.47 (2H, dt, J=13, 7 Hz), 2.93 (1H, dd J=14, 6 Hz), 3.16 (1H, dt, J=10, 7 Hz), 20 3.21 (1H, dd, J=14, 10 Hz), 3.57 (1H, d, J=5 Hz), 3.90 (1H, dt, J=10, 4 Hz), 4.19-4.33 (2H, m), 4.51-4.69 (2H, m), 5.11 (1H, dt, J=6, 10 Hz), 6.15 (1H, d, J=10 Hz), 6.55 (1H, d, J=10 Hz), 7.15 (1H, d, J=10 Hz), 7.18-7.36 (5H, m).

Example 249

25 Compound E249 was obtained from the Compound (461) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.38-1.73 (8H, m), 1.74 (3H, s), 1.95-2.30 (2H, m), 2.89-3.00 (1H, m), 2.95 (1H, d, J=13.6 Hz), 3.08-3.30 (2H, m), 3.16 (1H, d, J=13.6 Hz), 3.69-30 3.83 (1H, m), 4.06-4.21 (1H, m), 4.27 (1H, q, J=7.0 Hz), 4.57-4.66 (1H, m), 5.08-5.20 (1H, m), 6.08 (1H, s), 6.57 (1H, d, J=15.4 Hz), 6.84 (1H, dt, J=15.4, 7.0 Hz), 7.05 (1H, d, J=10.6 Hz), 7.16-7.47 (17H, m), 7.59 (1H, d, J=7.7 Hz), 7.59 (1H, d, J=8.1 Hz), 7.65 (1H, d, J=7.7 Hz), 7.65 (1H, d, J=8.1 Hz);

35 MASS (ES<sup>+</sup>): m/e 841.23 (M+1).

Example 250

Compound E250 was obtained from the Compound E249 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.13-1.83 (10H, m), 1.18 (3H, d, J=6.6 Hz), 1.73 (3H, s), 2.00-2.16 (1H, m), 2.19-2.31 (1H, m),  
5 2.43-2.53 (2H, m), 2.87-3.00 (1H, m), 2.94 (1H, d, J=13.5 Hz), 3.10-3.34 (2H, m), 3.15 (1H, d, J=13.5 Hz), 3.71-3.81 (1H, m), 4.06-4.19 (1H, m), 4.18 (1H, q, J=6.6 Hz), 4.58-4.66 (1H, m), 5.09-5.19 (1H, m), 6.05 (1H, s), 6.99 (1H, d, J=10.3 Hz), 7.17-7.48 (17H, m), 7.61 (2H, d, J=8.1 Hz), 7.64 (2H, d, J=8.1 Hz);  
10 MASS (ES+): m/e 843.28 (M+1).

Example 251

Compound E251 was obtained from the Compound E250 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.83 (10H, m), 1.38 (3H, d, J=7.0 Hz),  
15 1.73 (3H, s), 1.97-2.15 (1H, m), 2.16-2.31 (1H, m), 2.34-2.56 (2H, m), 2.89-3.00 (1H, m), 2.94 (1H, d, J=13.9 Hz), 3.08-3.30 (2H, m), 3.15 (1H, d, J=13.9 Hz), 3.55 (1H, d, J=4.4 Hz), 3.71-3.82 (1H, m), 4.07-4.28 (2H, m), 4.58-4.67 (1H, m), 5.07-5.21 (1H, m), 6.04 (1H, s), 7.01 (1H, d, J=9.5 Hz), 7.16-7.43 (10H, m), 7.38 (1H, d, J=10.3 Hz);  
20 MASS (ES+): m/e 605.37 (M+1).

Example 252

Compounds E23 (main product) and E252 (by-product) were obtained from the Compound E22 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): (for Compound E23) 0.81 (3H, t, J=7.3 Hz),  
25 1.22-1.41 (2H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.54-1.92 (8H, m), 2.06-2.57 (6H, m), 3.06 (1H, dd, J=13.9, 7.0 Hz), 3.24-3.36 (1H, m), 3.26 (1H, dd, J=13.9, 8.8 Hz), 3.55 (1H, d, J=4.8 Hz), 3.79-3.90 (2H, m), 4.15-4.29 (2H, m), 4.65-4.72 (1H, m), 5.18 (1H, ddd, J=10.3, 8.8, 7.0 Hz), 5.89 (1H, s), 6.99 (1H, d, J=10.3 Hz), 7.58 (2H, d, J=8.4 Hz), 7.35 (2H, d, J=8.4 Hz), 7.64 (1H, d, J=10.3 Hz);  
30 MASS (ES+): m/e 568.42 (M+1).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): (for Compound E252) 0.83 (3H, t, J=7.3 Hz), 1.22-1.41 (2H, m), 1.28 (3H, s), 1.38 (3H, t, J=7.0 Hz), 1.50-1.96 (8H, m), 2.08-2.40 (4H, m), 2.47 (2H, dt, J=12.5, 7.3 Hz), 3.03 (1H, dd, J=13.5, 6.2 Hz), 3.22-3.33 (1H, m), 3.25 (1H, dd, J=13.5, 9.2 Hz),  
35 3.80-3.89 (1H, m), 3.90 (1H, s), 4.17-4.30 (1H, m), 4.24 (1H, q, J=7.0

Hz), 4.64-4.70 (1H, m), 5.19 (1H, ddd, J=10.3, 9.2, 6.2 Hz), 5.85 (1H, s), 7.06 (1H, d, J=10.3 Hz), 7.31 (2H, d, J=8.4 Hz), 7.60 (1H, d, J=10.3 Hz), 7.95 (2H, d, J=8.4 Hz);  
MASS (ES+): m/e 601.46 (M+1).

5 Example 253

Compounds E252 (20 mg) was dissolved in methanol (0.3 ml) and the mixture was stirred at ambient temperature. To the mixture was added a 40% solution of N-methylamino metanol in methanol and the mixture was stirred under ambient temperature for 4 hours. The  
10 solvent and the residual agents were removed by evaporation, and the residue was purified by preparative chromatography (eluting with ethyl acetate/methanol=9/1) to give the objective Compound E253.  
<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.20-1.41 (2H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.49-1.89 (8H, m), 1.98-2.40 (4H, m),  
15 2.47 (2H, dt, J=11.7, 7.3 Hz), 3.00 (1H, dd, J=13.5, 6.2 Hz), 3.21-3.32 (1H, m), 3.27 (1H, dd, J=13.5, 9.5 Hz), 3.53-3.59 (1H, m), 3.79-3.90 (1H, m), 4.14-4.29 (2H, m), 4.63-4.69 (1H, m), 5.18 (1H, ddd, J=10.3, 9.5, 6.2 Hz), 5.90 (1H, s), 6.05-6.14 (1H, m), 7.06 (1H, d, J=10.3 Hz), 7.30 (2H, d, J=8.4 Hz), 7.60 (1H, d, J=10.3 Hz), 7.67 (2H, d, J=8.4 Hz);  
20

MASS (ES+): m/e 600.55 (M+1).

Example 254

Compound E254 was obtained from the Compound (453) in a manner similar to Example 1.  
25 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.7 Hz), 1.09 (9H, s), 1.22 (3H, d, J=7.0 Hz), 1.28 (3H, s), 1.38-1.90 (8H, m), 2.09-2.42 (4H, m), 3.04 (1H, dd, J=13.6, 6.2 Hz), 3.22-3.38 (1H, m), 3.31 (1H, dd, J=13.6, 9.9 Hz), 3.81-3.93 (1H, m), 4.17-4.33 (1H, m), 4.27 (1H, q, J=7.0 Hz), 4.65-4.72 (1H, m), 5.13-5.26 (1H, m), 5.83 (1H, s), 6.62 (1H, d, J=15.4 Hz),  
30 6.88 (1H, dt, J=15.4, 7.0 Hz), 7.04 (1H, d, J=10.3 Hz), 7.30-7.48 (7H, m), 7.51-7.76 (8H, m);

MASS (ES+): m/e 847.18 (M+1).

Example 255

Compound E255 was obtained from the Compound E254 in a manner  
35 similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.11 (9H, s), 1.18

(3H, d, J=6.6 Hz), 1.28 (3H, s), 1.38-1.90 (8H, m), 2.09-2.41 (4H, m), 2.46-2.57 (2H, m), 3.04 (1H, dd, J=13.6, 6.6 Hz), 3.22-3.36 (1H, m), 3.28 (1H, dd, J=13.6, 9.9 Hz), 3.80-3.92 (1H, m), 4.10-4.27 (1H, m), 4.19 (1H, q, J=6.6 Hz), 4.65-4.72 (1H, m), 5.13-5.27 (1H, m), 5.82 (1H, s), 7.00 (1H, d, J=10.3 Hz), 7.32-7.49 (7H, m), 7.54 (2H, d, J=8.4 Hz), 7.58-7.69 (5H, m), 7.69-7.76 (1H, m);  
MASS (ES+): m/e 849.25 (M+1).

#### Example 256

Compound E256 was obtained from the Compound E255 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, s), 1.17-1.43 (2H, m), 1.28 (3H, s), 1.38 (3H, d, J=7.3 Hz), 1.48-1.92 (8H, m), 2.06-2.59 (6H, m), 3.04 (1H, dd, J=13.9, 6.6 Hz), 3.22-3.37 (1H, m), 3.28 (1H, dd, J=13.9, 9.5 Hz), 3.57 (1H, d, J=4.8 Hz), 3.80-3.93 (1H, m), 4.15-4.30 (2H, m), 4.63-4.74 (1H, m), 5.13-5.28 (1H, m), 5.86 (1H, s), 7.03 (1H, d, J=9.9 Hz), 7.35 (2H, d, J=8.1 Hz), 7.54 (2H, d, J=8.1 Hz), 7.62 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 611.30 (M+1);

[α]<sub>D</sub><sup>25</sup> = -98.9° (c=0.475).

#### Example 257

Compound E257 was obtained from the Compound (469) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.17 (3H, s), 1.24 (3H, d, J=7.0 Hz), 1.41-1.99 (6H, m), 2.11-2.39 (4H, m), 3.09 (1H, dd, J=13.6, 6.6 Hz), 3.28-3.39 (1H, m), 3.29 (1H, dd, J=13.6, 8.8 Hz), 3.42 (1H, d, J=13.6 Hz), 3.60 (1H, d, J=13.6 Hz), 3.82-3.92 (1H, m), 4.16-4.25 (1H, m), 4.29 (1H, q, J=7.0 Hz), 4.66-4.73 (1H, m), 5.21-5.34 (1H, m), 5.91 (1H, s), 6.63 (1H, d, J=15.7 Hz), 6.89 (1H, dt, J=15.7, 6.6 Hz), 6.97-7.04 (2H, m), 7.13-7.21 (4H, m), 7.22-7.48 (11H, m), 7.57-7.69 (4H, m), 7.84 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 841.21 (M+1).

#### Example 258

Compound E258 was obtained from the Compound E257 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (9H, s), 1.17 (3H, s), 1.19 (3H, d, J=7.0 Hz), 1.41-1.69 (6H, m), 1.71-1.95 (4H, m), 2.09-2.40 (2H, m),

2.53 (2H, t, J=7.3 Hz), 3.08 (1H, dd, J=13.9, 7.0 Hz), 3.23-3.36 (1H, m), 3.29 (1H, dd, J=13.9, 9.1 Hz), 3.36 (1H, d, J=13.9 Hz), 3.64 (1H, d, J=13.9 Hz), 3.78-3.91 (1H, m), 4.12-4.23 (1H, m), 4.20 (1H, q, J=7.0 Hz), 4.64-4.73 (1H, m), 5.21-5.32 (1H, m), 5.86 (1H, s), 6.97-7.06 (2H, m), 7.11 (1H, d, J=10.3 Hz), 7.15-7.47 (14H, m), 7.56-7.68 (4H, m, J=10.3 Hz), 7.86 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 843.18 (M+1).

#### Example 259

Compound E259 was obtained from the Compound E258 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.17 (3H, s), 1.29-1.42 (3H, m), 1.39 (1H, d, J=7.3 Hz), 1.51-1.73 (4H, m), 1.73-1.98 (3H, m), 2.08-2.60 (4H, m), 3.09 (1H, dd, J=13.9, 7.0 Hz), 3.27-3.39 (1H, m), 3.29 (1H, dd, J=13.9, 8.8 Hz), 3.37 (1H, d, J=13.5 Hz), 3.56 (1H, d, J=4.0 Hz), 3.65 (1H, d, J=13.5 Hz), 3.81-3.92 (1H, m), 4.14-4.29 (2H, m), 4.67-4.74 (1H, m), 5.21-5.33 (1H, m), 5.87 (1H, s), 6.99-7.06 (2H, m), 7.14-7.35 (8H, m), 7.14 (1H, d, J=10.6 Hz), 7.85 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 605.38 (M+1);  
[α]<sub>D</sub><sup>26</sup> = -148.2° (c=0.55).

#### Example 260

Compound E260 was obtained from the Compound (105) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.3 Hz), 1.27 (3H, s), 1.30-1.55 (1H, m), 1.41 (6H, s), 1.56-1.92 (6H, m), 2.24-2.38 (6H, m), 2.02 (1H, s), 2.07-2.38 (6H, m), 2.96 (1H, dd, J=13.6, 2.2 Hz), 3.23 (1H, dd, J=13.6, 9.2 Hz), 3.20-3.32 (1H, m), 3.80-3.90 (1H, m), 4.20 (1H, ddd, J=15.4, 7.7, 7.7 Hz), 4.34 (2H, s), 4.63-4.69 (1H, brd, J=5.5 Hz), 5.18 (1H, ddd, J=17.6, 11.0, 7.7 Hz), 5.87 (1H, s), 6.79 (1H, d, J=15.4 Hz), 7.02 (1H, ddd, J=15.4, 6.6, 6.6 Hz), 7.12 (1H, d, J=10.3 Hz);  
MASS (ES+): m/e 667.3 (M+Na).

#### Example 261

Compound E261 was obtained from the Compound E260 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.28 (3H, t, J=7.3 Hz), 1.73 (3H, s), 1.65-1.87 (5H, m), 1.82 (6H, s), 2.00-2.34 (6H, m), 2.52-2.70 (2H, m),

2.70-2.85 (2H, m), 2.99 (2H, t, J=7.3 Hz), 3.41 (1H, dd, J=13.6, 6.2 Hz), 3.61-3.78 (2H, m), 4.23-4.39 (1H, m), 4.66 (1H, ddd, J=17.6, 7.7 Hz), 5.12 (1H, brd, J=6.2 Hz), 5.63 (1H, ddd, J=17.2, 14.3, 7.3 Hz), 6.40 (1H, s), 7.53-7.89 (6H, m, J=8 Hz), 8.02 (1H, brd, J=10.3 Hz);

5 MASS (ES+): m/e 557.3 (M+1).

Example 262

Compound E262 was obtained from the Compound (105) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.37-1.56 (2H, m), 1.56-1.94 (4H, m), 2.00-2.40 (6H, m), 2.56 (2H, q, J=7.3 Hz), 2.96 (1H, dd, J=13.6, 6.2 Hz), 3.16-3.33 (2H, m), 3.80-3.93 (1H, m), 4.23 (1H, ddd, J=15.8, 7.7, 7.7 Hz), 4.68 (1H, brd, J=5.9 Hz), 5.19 (1H, ddd, J=16.1, 9.9, 6.2 Hz), 5.92 (1H, s), 6.10 (1H, d, J=16.1 Hz), 6.79 (1H, dt, J=15.8, 7.0 Hz), 7.10-7.33 (6H, m), 7.54 (1H, brd, J=10.3 Hz);

15 MASS (ES+): m/e 525.7 (M+1).

Example 263

Compound E263 was obtained from the Compound (374) in a manner similar to Example 1.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.28 (3H, s), 1.43-1.58 (2H, m), 1.59-1.91 (3H, m), 2.10-2.37 (4H, m), 2.96 (1H, dd, J=13.6, 6.2 Hz), 3.16-3.37 (2H, m), 3.85 (1H, ddd, J=10.3, 10.3, 5.1 Hz), 4.25 (1H, ddd, J=10.3, 7.7, 7.7 Hz), 4.69 (1H, brd, J=5.5 Hz), 4.95 (2H, d, J=47.6 Hz), 5.17 (1H, ddd, J=16.5, 9.5, 6.5 Hz), 6.07 (1H, s), 6.35 (1H, brd, J=15.8 Hz), 6.83-7.08 (4H, m), 7.10-7.31 (5H, m), 7.58 (1H, d, J=9.9 Hz);

25 MASS (ES+): m/e 547.3 (M+1).

Example 264

Compound E264 was obtained from the Compound E263 in a manner similar to Example 3.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.21-1.42 (4H, m), 1.28 (3H, s), 1.53-1.70 (2H, m), 1.70-1.92 (4H, m), 2.08-2.39 (4H, m), 2.54 (2H, ddd, J=7.3, 7.3, 2.6 Hz), 2.96 (1H, dd, J=13.5, 6.2 Hz), 3.15-3.36 (2H, m), 3.86 (1H, ddd, J=10.2, 8.4, 4.8 Hz), 4.22 (1H, ddd, J=10.2, 7.7, 7.7 Hz), 4.69 (1H, brd, J=5.9 Hz), 4.80 (2H, d, J=47.6 Hz), 5.16 (1H, ddd, J=9.2, 9.2, 6.2 Hz), 6.00 (1H, s), 6.86-7.13 (5H,

m), 7.19-7.28 (1H, m), 7.61 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 549.4 (M+1).

Example 265

Compound E265 was obtained from the Compound (374) in a manner  
5 similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.21-1.40 (4H, m),  
1.28 (3H, s), 1.47-1.68 (3H, m), 1.69-1.90 (3H, m), 2.10-2.46 (4H, m),  
2.13 (3H, s), 2.54 (2H, ddd, J=7.3, 7.3, 2.9 Hz), 2.96 (1H, dd, J=13.5,  
6.6 Hz), 3.15-3.35 (2H, m), 3.85 (1H, ddd, J=10.3, 10.3, 5.1 Hz), 4.22  
10 (1H, ddd, J=10.3, 10.3, 8.1 Hz), 4.69 (1H, brd, J=6.6 Hz), 5.16 (1H,  
ddd, J=9.5, 9.5, 6.6 Hz), 6.09 (1H, s), 6.85-7.15 (4H, m), 7.18-7.28  
(1H, m), 7.62 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 531.4 (M+1).

Example 266

15 Compound E266 was obtained from the Compound (477) in a manner  
similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (1H, t, J=7.3 Hz), 1.09 (4H, s), 1.10  
(5H, s), 1.22 (3H, d, J=6.6 Hz), 1.29 (3H, s), 1.38-1.92 (8H, m),  
2.04-2.38 (6H, m), 2.93 (1H, dd, J=13.9, 6.6 Hz), 3.18 (1H, dd, J=13.9,  
20 9.2 Hz), 3.30 (1H, dt, J=10.3, 7.3 Hz), 3.80-3.90 (1H, m), 4.17-4.31  
(2H, m), 4.67-4.71 (1H, m), 5.12 (1H, ddd, J=9.8, 9.2, 6.6 Hz), 5.95  
(1H, s), 6.61 (1H, d, J=15.5 Hz), 6.8 (1H, dt, J=15.5, 6.6 Hz), 6.91-  
6.98 (1H, m), 7.01-7.12 (3H, m), 7.31-7.49 (6H, m), 7.55-7.70 (5H, m);  
MASS (ES+): m/e 815.46 (M+1).

25 Example 267

Compound E267 was obtained from the Compound E266 in a manner  
similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (9H, s), 1.18  
(3H, d, J=7.0 Hz), 1.29 (3H, s), 1.36-1.91 (10H, m), 2.08-2.38 (4H, m),  
30 2.51 (2H, dt, J=7.0, 2.6 Hz), 2.92 (1H, dd, J=13.5, 6.2 Hz), 3.18 (1H,  
dd, J=13.5, 9.5 Hz), 3.30 (1H, dt, J=10.3, 8.0 Hz), 3.80-3.89 (1H, m),  
4.14-4.27 (1H, m), 4.19 (1H, q, J=7.0 Hz), 4.66-4.72 (1H, m), 5.11 (1H,  
ddd, J=9.5, 9.2, 6.6 Hz), 5.82 (1H, s), 6.91-6.99 (1H, m), 7.00-7.11  
(3H, m), 7.33-7.48 (6H, m), 7.58-7.67 (5H, m);

35 MASS (ES+): m/e 817.45 (M+1).

Example 268

Compound E268 was obtained from the Compound E267 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.23-1.41 (5H, m), 1.29 (3H, s), 1.52-1.97 (8H, m), 2.06-2.58 (6H, m), 2.92 (1H, dd, J=13.6, 6.6 Hz), 3.18 (1H, dd, J=13.6, 9.2 Hz), 3.31 (1H, dt, J=10.3, 7.3 Hz), 3.59 (1H, d, J=4.0 Hz), 3.80-3.90 (1H, m), 4.16-4.29 (2H, m), 4.65-4.73 (1H, m), 5.12 (1H, ddd, J=9.9, 9.5, 6.6 Hz), 5.92 (1H, s), 6.91-6.99 (1H, m), 7.00-7.12 (3H, m), 7.60 (1H, d, J=10.3 Hz);

MASS (ES<sup>+</sup>): m/e 579.55 (M+1).

10 Example 269

Compound E269 was obtained from the Compound (483) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.09 (3x3H, s), 1.18-1.92 (12H, m), 1.22 (3H, d, J=7 Hz), 1.28 (3H, s), 2.08-2.40 (6H, m), 2.58 (2H, m), 2.86-2.98 (3H, m), 3.21 (1H, dd, J=13.5, 9.5 Hz), 3.23-3.37 (3H, m), 3.55 (2H, m), 3.88 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7 Hz), 4.68 (1H, dd, J=7.5, 2 Hz), 5.17 (1H, m), 5.89 (1H, s), 6.62 (1H, d, J=15.8 Hz), 6.87 (1H, dt, J=15.8, 7 Hz), 7.08-7.18 (5H, m), 7.31-7.48 (6H, m), 7.53 (1H, d, J=10 Hz), 7.56-7.69 (4H, m);

20 MASS (ES<sup>+</sup>): m/e 918.56.

Example 270

Compound E270 was obtained from the Compound E269 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.18 (3H, d, J=7 Hz), 1.18-1.32 (4H, m), 1.28 (3H, s), 1.39-1.89 (12H, m), 2.08-2.40 (4H, m), 2.46-2.62 (4H, m), 2.86-2.98 (3H, m), 3.20 (1H, dd, J=13.5, 9.5 Hz), 3.22-3.37 (3H, m), 3.55 (2H, m), 3.86 (1H, m), 4.18 (1H, m), 4.18 (1H, q, J=7 Hz), 4.68 (1H, m), 5.16 (1H, m), 5.89 (1H, s), 7.08 (1H, d, J=10.3 Hz), 7.08-7.18 (4H, m), 7.32-7.48 (6H, m), 7.57 (1H, d, J=10.3 Hz), 7.57-7.66 (4H, m);

30 MASS (ES<sup>-</sup>): m/e 954.65 (M+Cl).

Example 271

Compound E271 was obtained from the Compound E270 in a manner similar to Example 6.

35 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.20-1.40 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.42-1.89 (12H, m), 2.07-2.62 (8H,

m), 2.83-2.97 (3H, m), 3.20 (1H, dd, J=13.5, 9.5 Hz), 3.23-3.37 (3H, m), 3.50-3.59 (3H, m), 3.87 (1H, m), 4.14-4.28 (2H, m), 4.68 (1H, m), 5.16 (1H, m), 5.91 (1H, s), 7.07-7.19 (5H, m), 7.55 (1H, d, J=10 Hz); MASS (ES+): m/e 682.57.

5 Example 272

Compound E272 was obtained from the Compound (486) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.09 (3x3H, s), 1.22 (3H, t, J=7 Hz), 1.27 (3H, s), 1.38-1.51 (2H, m), 1.56-1.91 (4H, m), 2.07-2.38 (6H, m), 2.63 (2H, t, J=7.5 Hz), 2.94 (1H, dd, J=14, 6.5 Hz), 3.01 (2H, t, J=7.5 Hz), 3.20 (1H, dd, J=14, 9.5 Hz), 3.25 (1H, m), 3.85 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7 Hz), 4.66 (1H, m), 5.15 (1H, ddd, J=10, 9.5, 6.5 Hz), 5.89 (1H, s), 6.61 (1H, d, J=16 Hz), 6.86 (1H, dt, J=16, 7 Hz), 7.01-7.21 (7H, m), 7.26-7.49 (8H, m), 7.53 (1H, d, J=10 Hz), 7.57-7.70 (6H, m); MASS (ES+): m/e 926.49.

Example 273

Compound E273 was obtained from the Compound E272 in a manner similar to Example 3.

20 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.4 Hz), 1.10 (3x3H, s), 1.16-1.32 (4H, m), 1.18 (3H, d, J=7 Hz), 1.27 (3H, s), 1.38-1.64 (3H, m), 1.67-1.85 (3H, m), 2.08-2.38 (4H, m), 2.51 (2H, m), 2.63 (2H, t, J=7.3 Hz), 2.94 (1H, dd, J=13.5, 6 Hz), 3.01 (2H, t, J=7.3 Hz), 3.20 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.84 (1H, m), 4.08-4.24 (2H, m), 4.66 (1H, m), 5.15 (1H, m), 5.88 (1H, s), 7.00-7.20 (7H, m), 7.25-7.50 (10H, m), 7.54-7.70 (5H, m); MASS (ES+): m/e 928.42.

Example 274

30 Compound E274 was obtained from the Compound E273 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.82 (3H, t, J=7.3 Hz), 1.20-1.41 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.52-1.88 (6H, m), 2.05-2.57 (6H, m), 2.63 (2H, t, J=7.5 Hz), 2.93 (1H, dd, J=14, 6 Hz), 3.01 (2H, t, J=7.5 Hz), 3.20 (1H, dd, J=14, 9.5 Hz), 3.26 (1H, m), 3.56 (1H, brd, J=5 Hz), 3.84 (1H, m), 4.14-4.28 (2H, m), 4.66 (1H, dd, J=8, 2 Hz), 5.15 (1H, ddd, J=10.3, 9.5, 6 Hz), 5.91 (1H, s), 7.02-7.20 (7H, m),

7.30 (2x1H, dd, J=7.5, 7.5 Hz), 7.43 (2x1H, d, J=7.5 Hz), 7.55 (1H, d, J=10.3 Hz);

MASS (ES+): m/e 690.49;

$[\alpha]_D^{25} = -104.0^\circ$  (c=0.21, CHCl<sub>3</sub>).

5 Example 275

Compound E275 was obtained from the Compound (498) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (3x3H, s), 1.16-1.86 (8H, m), 1.23 (3H, d, J=7 Hz), 1.90-2.27 (4H, m), 3.01 (1H, m), 3.08 (1H, dd, J=14, 7 Hz),  
10 3.23 (1H, dd, J=13.5, 6 Hz), 3.26 (1H, dd, J=14, 8 Hz), 3.62 (1H, dd, J=13.5, 10.5 Hz), 3.74 (1H, m), 3.96 (1H, m), 4.17 (1H, m), 4.28 (1H, q, J=7 Hz), 5.01 (1H, m), 5.36 (1H, m), 6.45 (1H, d, J=6 Hz), 6.46 (1H, d, J=10 Hz), 6.59 (1H, d, J=15.7, 7 Hz), 6.82 (1H, dt, J=15.7, 7 Hz), 7.06-7.12 (2H, m), 7.15-7.50 (15H, m), 7.56-7.69 (4H, m);

15 MASS (ES+): m/e 841.34.

Example 276

Compound E276 was obtained from the Compound E275 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.12-1.29 (4H, m), 1.29 (3H, d, J=7 Hz), 1.36-1.81 (8H, m), 1.91-2.18 (2H, m), 2.50 (2H, m), 3.01  
20 (1H, m), 3.08 (1H, dd, J=14, 7 Hz), 3.15-3.30 (2H, m), 3.58-3.77 (2H, m), 3.94 (1H, m), 4.11-4.23 (2H, m), 5.01 (1H, m), 5.35 (1H, m), 6.42 (1H, d, J=6.5 Hz), 6.43 (1H, d, J=9.5 Hz), 7.05-7.13 (2H, m), 7.15-7.49 (15H, m), 7.57-7.67 (4H, m);

25 MASS (ES+): m/e 843.58.

Example 277

Compound E277 was obtained from the Compound E276 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.40 (6H, m), 1.38 (3H, d, J=7 Hz),  
30 1.44-1.85 (6H, m), 1.97 (1H, m), 2.09 (1H, m), 2.33-2.56 (2H, m), 3.01 (1H, m), 3.08 (1H, dd, J=14, 7 Hz), 3.21 (1H, dd, J=13, 6 Hz), 3.25 (1H, dd, J=14, 8 Hz), 3.58 (1H, d, J=4.5 Hz), 3.64 (1H, dd, J=13, 11 Hz), 3.73 (1H, m), 3.95 (1H, m), 4.10-4.29 (2H, m), 5.02 (1H, m), 5.35 (1H, m), 6.41-6.52 (2H, m), 7.06-7.14 (8H, m), 7.16-7.34 (8H, m), 7.44  
35 (1H, d, J=10 Hz);

MASS (ES+): m/e 605.36.

Example 278

Compound E278 was obtained from the Compound (498) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.24 (3H, d, J=7 Hz), 1.29-  
5 1.86 (8H, m), 1.90-2.27 (4H, m), 3.01 (1H, m), 3.08 (1H, dd, J=14, 7  
Hz), 3.18-3.31 (2H, m), 3.61 (1H, dd, J=13, 10.5 Hz), 3.72 (1H, m),  
3.96 (1H, m), 4.16 (1H, m), 4.28 (1H, q, J=7 Hz), 5.01 (1H, m), 5.36  
(1H, m), 6.40 (1H, d, J=5 Hz), 6.46 (1H, d, J=10 Hz), 6.60 (1H, d,  
J=15.8 Hz), 6.82 (1H, dt, J=15.8, 7 Hz), 7.05-7.12 (2H, m), 7.16-7.48  
10 (15H, m), 7.56-7.70 (4H, m);  
MASS (ES-): m/e 839.43.

Example 279

Compound E279 was obtained from the Compound E278 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.14-1.29 (4H, m), 1.19 (3H,  
15 d, J=7 Hz), 1.37-1.63 (6H, m), 1.67-1.82 (2H, m), 2.50 (2H, m), 3.02  
(2H, m), 3.08 (1H, dd, J=13.5, 7 Hz), 3.21 (1H, dd, J=13.5, 4.5 Hz),  
3.26 (1H, dd, J=13.5, 8 Hz), 3.64 (1H, dd, J=13.5, 10.5 Hz), 3.72 (1H,  
ddd, J=8, 5, 4.5 Hz), 3.95 (1H, m), 4.16 (1H, m), 4.19 (1H, q, J=7 Hz),  
20 5.01 (1H, m), 5.36 (1H, m), 6.39 (1H, d, J=5 Hz), 6.42 (1H, d, J=10.5  
Hz), 7.07-7.13 (2H, m), 7.16-7.50 (15H, m), 7.58-7.69 (4H, m);  
MASS (ES+): m/e 843.41.

Example 280

Compound E280 was obtained from the Compound E279 in a manner  
25 similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.12-1.42 (6H, m), 1.38 (3H, d, J=7 Hz),  
1.44-1.85 (6H, m), 1.97 (1H, m), 2.08 (1H, m), 2.32-2.56 (2H, m), 3.01  
(1H, m), 3.08 (1H, dd, J=14, 7 Hz), 3.21 (1H, dd, J=13, 6 Hz), 3.25  
(1H, dd, J=14, 8 Hz), 3.58 (1H, d, J=5 Hz), 3.64 (1H, dd, J=13, 11 Hz),  
30 3.73 (1H, ddd, J=11, 6, 6 Hz), 3.95 (1H, m), 4.10-4.28 (2H, m), 5.02  
(1H, m), 5.36 (1H, ddd, J=10.5, 8, 7 Hz), 6.47 (1H, d, J=10 Hz), 6.53  
(1H, d, J=6 Hz), 7.07-7.15 (2H, m), 7.17-7.35 (8H, m), 7.45 (1H, d,  
J=10.5 Hz);  
MASS (ES+): m/e 605.28.

35 Example 281

Compound E281 was obtained from the Compound (507) in a manner

similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.16-1.28 (2H, m), 1.24 (3H, d, J=7 Hz), 1.30-1.44 (2H, m), 1.70-1.91 (2H, m), 2.10-2.36 (4H, m), 3.03 (1H, dd, J=13.5, 6.3 Hz), 3.16-3.38 (3H, m), 3.60-3.80 (2H, m), 3.87 (1H, m), 4.16 (1H, m), 4.27 (1H, m), 4.67 (1H, m), 5.17 (1H, m), 6.37 (1H, d, J=5.5 Hz), 6.60 (1H, d, J=15.7 Hz), 6.84 (1H, dt, J=15.7, 7 Hz), 7.09-7.54 (18H, m), 7.56-7.74 (4H, m);  
MASS (ES<sup>+</sup>): m/e 828.12.

Example 282

Compound E282 was obtained from the Compound E281 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.15-1.28 (4H, m), 1.19 (3H, d, J=6.5 Hz), 1.38-1.64 (3H, m), 1.69-1.86 (3H, m), 2.13-2.36 (2H, m), 2.50 (2H, m), 3.02 (1H, dd, J=13.5, 6.3 Hz), 3.18-3.35 (3H, m), 3.62-3.79 (2H, m), 3.86 (1H, m), 4.13 (1H, m), 4.19 (1H, q, J=6.5 Hz), 4.68 (1H, m), 5.16 (1H, m), 6.33 (1H, d, J=6 Hz), 7.07 (1H, d, J=10 Hz), 7.10-7.16 (2H, m), 7.19-7.49 (14H, m), 7.53 (1H, d, J=10 Hz), 7.58-7.70 (4H, m);  
MASS (ES<sup>+</sup>): m/e 829.77.

Example 283

Compound E283 was obtained from the Compound E282 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.41 (4H, m), 1.38 (3H, d, J=7 Hz), 1.47-1.89 (6H, m), 2.06-2.56 (4H, m), 3.02 (1H, dd, J=13.5, 6.3 Hz), 3.22 (1H, m), 3.27 (1H, dd, J=13.5, 9.5 Hz), 3.31 (1H, dd, J=13, 6 Hz), 3.59 (1H, d, J=4.8 Hz), 3.67 (1H, dd, J=13, 10.5 Hz), 3.74 (1H, ddd, J=10.5, 6, 5.5 Hz), 3.86 (1H, m), 4.16 (1H, m), 4.24 (1H, dq, J=7, 4.8 Hz), 4.68 (1H, m), 5.16 (1H, ddd, J=10.3, 9.5, 6.3 Hz), 6.49 (1H, d, J=5.5 Hz), 7.08-7.34 (11H, m), 7.53 (1H, d, J=10.3 Hz);  
MASS (ES<sup>+</sup>): m/e 591.37.

Example 284

Compound E284 was obtained from the Compound (507) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.34-1.45 (2H, m), 1.52-1.91 (4H, m), 2.12-2.34 (4H, m), 3.00 (1H, dd, J=13.5, 6 Hz), 3.19-3.36 (3H, m), 3.59-3.79 (2H, m), 3.86 (1H, m), 4.16 (1H, m), 4.33 (2H,

s), 4.67 (1H, m), 5.16 (1H, m), 6.34 (1H, d, J=5.8 Hz), 6.41 (1H, d, J=15.8 Hz), 6.86 (1H, dt, J=15.8, 7 Hz), 7.09-7.54 (18H, m), 7.62-7.74 (4H, m);

MASS (ES+): m/e 813.66.

5 Example 285

Compound E285 was obtained from the Compound E284 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.16-1.32 (4H, m), 1.46-1.88 (6H, m), 2.11-2.38 (2H, m), 2.47 (3H, t, J=7.3 Hz), 3.02 (1H, dd, J=14, 6 Hz), 3.20-3.35 (3H, m), 3.62-3.80 (2H, m), 3.86 (1H, m), 4.14 (1H, m), 4.17 (2H, s), 4.67 (1H, m), 5.14 (1H, m), 6.36 (1H, d, J=5.5 Hz), 7.08 (1H, d, J=10.5 Hz), 7.08-7.49 (16H, m), 7.54 (1H, d, J=10.5 Hz), 7.61-7.71 (4H, m);

MASS (ES+): m/e 815.51..

15 Example 286

Compound E286 was obtained from the Compound E285 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.16-1.38 (4H, m), 1.48-1.90 (6H, m), 2.10-2.43 (4H, m), 3.02 (1H, dd, J=13.5, 6 Hz), 3.15 (1H, t, J=4 Hz), 3.22 (1H, m), 3.27 (1H, dd, J=13.5, 9.5 Hz), 3.31 (1H, dd, J=12.5, 5.5 Hz), 3.67 (1H, dd, J=12.5, 10 Hz), 3.74 (1H, ddd, J=10, 5.5, 5 Hz), 3.86 (1H, m), 4.15 (1H, m), 4.24 (2H, d, J=4 Hz), 4.68 (1H, m), 5.16 (1H, ddd, J=10.5, 9.5, 6 Hz), 6.44 (1H, d, J=5 Hz), 7.06-7.35 (11H, m), 7.52 (1H, d, J=10.5 Hz);

25 MASS (ES+): m/e 577.38.

Example 287

Compound E287 was obtained from the Compound (517) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (3x3H, s), 1.16-1.85 (4H, m), 1.23 (3H, d, J=7 Hz), 1.38 (3H, t, J=7 Hz), 1.90-2.26 (4H, m), 2.92-3.30 (4H, m), 3.53 (1H, dd, J=14, 10 Hz), 3.68 (1H, m), 3.95 (1H, m), 3.96 (2H, q, J=7 Hz), 4.18 (1H, m), 4.28 (1H, q, J=7 Hz), 5.01 (1H, m), 5.36 (1H, m), 6.46 (1H, d, J=10 Hz), 6.47 (1H, d, J=5 Hz), 6.61 (1H, d, J=16 Hz), 6.74 (2x1H, d, J=8.5 Hz), 6.83 (1H, dt, J=16, 7 Hz), 6.97 (2x1H, d, J=8.5 Hz), 7.19-7.48 (12H, m), 7.55-7.70 (4H, m);

35 MASS (ES+): m/e 885.32.

Example 288

Compound E288 was obtained from the Compound E287 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.14-1.24 (4H, m), 1.19 (3H, d, J=7 Hz), 1.34-1.63 (6H, m), 1.38 (3H, t, J=7 Hz), 1.67-1.80 (2H, m), 1.97 (1H, m), 2.10 (1H, m), 2.51 (2H, m), 3.02 (1H, m), 3.08 (1H, dd, J=14, 7.5 Hz), 3.16 (1H, dd, J=13.5, 6.5 Hz), 3.25 (1H, dd, J=14, 8 Hz), 3.56 (1H, dd, J=13.5, 6.5 Hz), 3.67 (1H, ddd, J=10.5, 7, 6.5 Hz), 3.95 (1H, m), 3.98 (2H, q, J=7 Hz), 4.16 (1H, m), 4.19 (1H, q, J=7 Hz), 5.02 (1H, m), 5.35 (1H, m), 6.39 (1H, d, J=7 Hz), 6.43 (1H, d, J=10.5 Hz), 6.76 (2x1H, d, J=8.5 Hz), 6.99 (2x1H, d, J=8.5 Hz), 7.20-7.50 (12H, m), 7.59-7.68 (4H, m);

MASS (ES<sup>+</sup>): m/e 887.32.

Example 289

Compound E289 was obtained from the Compound E288 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.42 (4H, m), 1.38 (3H, d, J=7 Hz), 1.39 (3H, t, J=7 Hz), 1.44-1.84 (8H, m), 1.90-2.18 (2H, m), 2.45 (2H, m), 3.01 (1H, m), 3.07 (1H, dd, J=14, 7.5 Hz), 3.15 (1H, dd, J=13.5, 6 Hz), 3.25 (1H, dd, J=14, 8 Hz), 3.56 (1H, m), 3.57 (1H, d, J=4.5 Hz), 3.68 (1H, m), 3.95 (1H, m), 3.98 (2H, q, J=7 Hz), 4.16 (1H, m), 4.22 (1H, dq, J=7, 4.5 Hz), 5.01 (1H, m), 5.35 (1H, ddd, J=10, 8, 7.5 Hz), 6.42 (1H, d, J=6.5 Hz), 6.45 (1H, d, J=10 Hz);

MASS (ES<sup>+</sup>): m/e 649.28.

Example 290

Compound E290 was obtained from the Compound (529) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (3x3H, s), 1.16-1.86 (8H, m), 1.23 (3H, d, J=7 Hz), 1.38 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 1.91-2.25 (4H, m), 2.92-3.06 (2H, m), 3.12-3.25 (2H, m), 3.54 (1H, dd, J=14, 10 Hz), 3.68 (1H, m), 3.97 (1H, m), 4.18 (1H, m), 4.28 (1H, q, J=7 Hz), 5.01 (1H, m), 5.30 (1H, m), 6.34 (1H, d, J=6 Hz), 6.45 (1H, d, J=10 Hz), 6.62 (1H, d, J=15.7 Hz), 6.75 (2x1H, d, J=8.5 Hz), 6.82 (2x1H, d, J=8.5 Hz), 6.83 (1H, m), 6.98 (2x1H, d, J=8.5 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.30-7.50 (7H, m), 7.56-7.74 (4H, m);

MASS (ES<sup>+</sup>): m/e 929.47.

Example 291

Compound E291 was obtained from the Compound E290 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.14-1.64 (10H, m), 1.19  
5 (3H, d, J=7 Hz), 1.38 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 1.66-1.81  
(2H, m), 1.92-2.15 (2H, m), 2.50 (2H, m), 2.94-3.07 (2H, m), 3.12-3.23  
(2H, m), 3.55 (1H, dd, J=13, 10.5 Hz), 3.67 (1H, m), 3.94 (1H, m),  
3.98 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.15 (1H, m), 4.19 (1H, q,  
J=7 Hz), 5.01 (1H, m), 5.30 (1H, m), 6.32 (1H, d, J=6 Hz), 6.41 (1H, d,  
10 J=10 Hz), 6.76 (2x1H, d, J=8.5 Hz), 6.82 (2x1H, d, J=8.5 Hz), 6.99  
(2x1H, d, J=8.5 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.32-7.48 (7H, m),  
7.58-7.69 (4H, m);  
MASS (ES<sup>+</sup>): m/e 931.60.

Example 292

15 Compound E292 was obtained from the Compound E291 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.14-1.65 (10H, m), 1.38 (3H, d, J=7 Hz),  
1.39 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 1.67-1.84 (2H, m), 1.91-  
2.14 (2H, m), 2.33-2.54 (2H, m), 2.92-3.06 (2H, m), 3.10-3.23 (2H, m),  
20 3.56 (1H, dd, J=12, 10.5 Hz), 3.57 (1H, d, J=5 Hz), 3.67 (1H, m), 3.94  
(1H, m), 3.98 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.16 (1H, m),  
4.22 (1H, dq, J=7, 5 Hz), 5.01 (1H, m), 5.30 (1H, m), 6.33 (1H, d, J=6  
Hz), 6.44 (1H, d, J=10.5 Hz), 6.76 (2x1H, d, J=8.7 Hz), 6.82 (2x1H, d,  
J=8.7 Hz), 6.99 (2x1H, d, J=8.7 Hz), 7.15 (2x1H, d, J=8.7 Hz), 7.37  
25 (1H, d, J=10 Hz);  
MASS (ES<sup>+</sup>): m/e 693.48.

Example 293

Compound E293 was obtained from the Compound (527) in a manner similar to Example 1.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.20-2.26 (12H, m), 1.37  
(3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 2.93-3.06 (2H, m), 3.12-3.24  
(2H, m), 3.53 (1H, dd, J=13.5, 10.5 Hz), 3.67 (1H, m), 3.95 (1H, m),  
3.96 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.16 (1H, m), 4.33 (2H, s),  
5.00 (1H, m), 5.30 (1H, m), 6.33 (1H, d, J=6 Hz), 6.44 (1H, d, J=16  
35 Hz), 6.45 (1H, d, J=10 Hz), 6.74 (2x1H, d, J=8.7 Hz), 6.82 (2x1H, d,  
J=8.7 Hz), 6.85 (1H, dt, J=16, 7 Hz), 6.97 (2x1H, d, J=8.7 Hz), 7.15

(2x1H, d, J=8.7 Hz), 7.32-7.48 (7H, m), 7.61-7.73 (4H, m);

MASS (ES+): m/e 915.52.

Example 294

Compound E294 was obtained from the Compound E293 in a manner  
5 similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.15-1.30 (4H, m), 1.38 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 1.44-1.65 (6H, m), 1.67-1.80 (2H, m), 1.92-2.14 (2H, m), 2.47 (2H, t, J=7.3 Hz), 2.93-3.07 (2H, m), 3.11-3.23 (2H, m), 3.55 (1H, dd, J=13.5, 10.8 Hz), 3.66 (1H, m), 3.94 (1H, m), 3.97 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.15 (1H, m), 4.17 (2H, s), 5.01 (1H, m), 5.29 (1H, m), 6.32 (1H, d, J=5.8 Hz), 6.42 (1H, d, J=10.5 Hz), 6.76 (2x1H, d, J=8.8 Hz), 6.82 (2x1H, d, J=8.8 Hz), 6.99 (2x1H, d, J=8.8 Hz), 7.15 (2x1H, d, J=8.8 Hz), 7.34-7.49 (7H, m), 7.61-7.69 (4H, m);

15 MASS (ES+): m/e 917.56.

Example 295

Compound E295 was obtained from the Compound E294 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.06-2.30 (14H, m), 1.39 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 2.38 (2H, t, J=7 Hz), 2.90-3.07 (2H, m), 3.09-3.28 (2H, m), 3.54 (1H, dd, J=13, 10 Hz), 3.69 (1H, m), 3.94 (1H, m), 3.98 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.18 (1H, m), 4.23 (2H, s), 5.02 (1H, m), 5.29 (1H, m), 6.42-6.52 (1H, m), 6.76 (2x1H, d, J=8.5 Hz), 6.82 (2x1H, d, J=8.5 Hz), 7.00 (2x1H, d, J=8.5 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.39 (2x1H, d, J=10 Hz);

25 MASS (ES+): m/e 679.40.

Example 296

Compound E296 was obtained from the Compound (527) in a manner similar to Example 1.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.80 (3H, t, J=7.5 Hz), 1.11 (3x3H, s), 1.20-1.82 (10H, m), 1.38 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 1.91-2.22 (4H, m), 2.94-3.06 (2H, m), 3.13-3.24 (2H, m), 3.53 (1H, dd, J=13.5, 10.5 Hz), 3.68 (1H, m), 3.95 (1H, m), 3.97 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.10-4.22 (2H, m), 5.01 (1H, m), 5.30 (1H, m), 35 6.33 (1H, d, J=6 Hz), 6.44 (1H, d, J=10.5 Hz), 6.55 (1H, d, J=16 Hz), 6.74 (1H, m), 6.75 (2x1H, d, J=8.5 Hz), 6.82 (2x1H, d, J=8.5 Hz), 6.98

(2x1H, d, J=8.5 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.29-7.48 (7H, m),  
7.56-7.68 (4H, m);

MASS (ES+): m/e 943.60.

Example 297

5           Compound E297 was obtained from the Compound E296 in a manner  
similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.81 (3H, t, J=7.5 Hz), 1.05-1.78 (14H, m),  
1.11 (3x3H, s), 1.38 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 1.90-2.14  
(2H, m), 2.38 (2H, m), 2.94-3.07 (2H, m), 3.11-3.23 (2H, m), 3.55 (1H,  
10 dd, J=13, 10 Hz), 3.66 (1H, m), 3.93 (1H, m), 3.97 (2H, q, J=7 Hz),  
4.00 (2H, q, J=7 Hz), 4.06-4.18 (2H, m), 5.01 (1H, m), 5.29 (1H, m),  
6.28 (1H, d, J=5.5 Hz), 6.40 (1H, d, J=10 Hz), 6.76 (2x1H, d, J=8.5  
Hz), 6.82 (2x1H, d, J=8.5 Hz), 6.98 (2x1H, d, J=8.5 Hz), 7.15 (2x1H, d,  
J=8.5 Hz), 7.31-7.47 (7H, m), 7.57-7.67 (4H, m);

15       MASS (ES+): m/e 945.55.

Example 298

          Compound E298 was obtained from the Compound E297 in a manner  
similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.94 (3H, t, J=7.3 Hz), 1.14-1.43 (6H, m),  
20 1.39 (3H, t, J=7 Hz), 1.40 (3H, t, J=7 Hz), 1.46-2.16 (8H, m), 2.43  
(2H, m), 2.92-3.06 (2H, m), 3.16 (1H, dd, J=13, 6 Hz), 3.18 (1H, dd,  
J=13.5, 7.5 Hz), 3.52 (1H, d, J=5 Hz), 3.55 (1H, m), 3.67 (1H, m),  
3.94 (1H, m), 3.98 (2H, q, J=7 Hz), 4.00 (2H, q, J=7 Hz), 4.10-4.22  
(2H, m), 5.01 (1H, m), 5.29 (1H, m), 6.40 (1H, d, J=5.5 Hz), 6.45 (1H,  
25 d, J=10 Hz), 6.76 (2x1H, d, J=8.7 Hz), 6.81 (2x1H, d, J=8.7 Hz), 6.99  
(2x1H, d, J=8.7 Hz), 7.15 (2x1H, d, J=8.7 Hz), 7.38 (1H, d, J=10.5  
Hz);

MASS (ES+): m/e 707.42.

Example 299

30           Compound E299 was obtained from the Compound (537) in a manner  
similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (3x3H, s), 1.22 (3H, d, J=6.5 Hz),  
1.35-1.50 (2H, m), 1.39 (3H, t, J=7 Hz), 1.58-1.88 (4H, m), 2.11-2.39  
(4H, m), 2.76 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13.5, 5.5 Hz),  
35 3.02-3.24 (3H, m), 3.95 (1H, m), 3.99 (2H, q, J=7 Hz), 4.25 (1H, m),  
4.26 (1H, q, J=6.5 Hz), 4.61 (1H, dd, J=8, 2 Hz), 4.68 (1H, m), 5.06

(1H, m), 6.33 (1H, d, J=10 Hz), 6.45 (1H, d, J=10.5 Hz), 6.59 (1H, d, J=16 Hz), 6.80 (2x1H, d, J=8.7 Hz), 6.84 (1H, dt, J=16, 7 Hz), 7.11 (2x1H, d, J=8.7 Hz), 7.15-7.48 (12H, m), 7.56-7.70 (4H, m);

MASS (ES+): m/e 871.38.

5 Example 300

Compound E300 was obtained from the Compound E299 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.14-1.28 (4H, m), 1.18 (3H, d, J=7 Hz), 1.33-1.50 (2H, m), 1.39 (3H, t, J=7 Hz), 1.54-1.82 (4H, m),  
10 2.20 (1H, m), 2.32 (1H, m), 2.49 (2H, m), 2.76 (1H, dd, J=14, 7 Hz),  
2.86 (1H, dd, J=13.5, 5 Hz), 3.02-3.24 (3H, m), 3.94 (1H, m), 3.99 (2H, q, J=7 Hz), 4.18 (1H, q, J=7 Hz), 4.24 (1H, m), 4.61 (1H, dd, J=8, 2.5 Hz), 4.68 (1H, m), 5.06 (1H, m), 6.31 (1H, d, J=10 Hz), 6.47 (1H, d, J=10.5 Hz), 6.80 (2x1H, d, J=9 Hz), 6.98-7.30 (8H, m), 7.32-7.48 (6H,  
15 m), 7.58-7.68 (4H, m);

MASS (ES+): m/e 873.47.

Example 301

Compound E301 was obtained from the Compound E300 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.19-1.35 (4H, m), 1.38 (3H, d, J=7.3 Hz), 1.40 (3H, d, J=7 Hz), 1.52-1.88 (6H, m), 2.12-2.56 (4H, m), 2.77 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13, 5 Hz), 3.01-3.24 (3H, m), 3.56 (1H, br), 3.94 (1H, m), 4.00 (2H, q, J=7 Hz), 4.17-4.30 (2H, m), 4.61 (1H, dd, J=8, 3 Hz), 4.68 (1H, m), 5.06 (1H, m), 6.36 (1H, d, J=10 Hz),  
25 6.48 (1H, d, J=10.5 Hz), 6.80 (2x1H, d, J=8.5 Hz), 7.11 (2x1H, d, J=8.5 Hz), 7.13-7.32 (6H, m);

MASS (ES+): m/e 635.

Example 302

Compound E302 was obtained from the Compound (545) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.09 (3x3H, s), 1.22 (3H, d, J=7 Hz), 1.34-1.51 (2H, m), 1.57-1.88 (4H, m), 2.10-2.39 (4H, m), 2.84 (1H, dd, J=14, 7 Hz), 2.88 (1H, dd, J=13, 5 Hz), 3.08 (1H, m), 3.19 (1H, dd, J=13, 10.5 Hz), 3.22 (1H, dd, J=14, 8 Hz), 3.94 (1H, m), 4.26 (1H, m), 4.27 (1H, q, J=7 Hz), 4.61 (1H, dd, J=8, 2.5 Hz), 4.75 (1H, ddd, J=10, 8, 7 Hz), 5.07 (1H, ddd, J=10.5, 10.5, 5 Hz), 6.37 (1H, d, J=10 Hz), 6.48

(1H, d, J=10.5 Hz), 6.58 (1H, d, J=16 Hz), 6.84 (1H, dt, J=16, 7 Hz), 7.14-7.48 (17H, m), 7.55-7.69 (4H, m);

MASS (ES+): m/e 827.56.

#### Example 303

5 Compound E303 was obtained from the Compound E302 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.10 (3x3H, s), 1.15-1.30 (4H, m), 1.18 (3H, d, J=7 Hz), 1.36-1.50 (2H, m), 1.52-1.84 (4H, m), 2.12-2.40 (2H, m), 2.48 (2H, m), 2.84 (1H, dd, J=14, 7 Hz), 2.87 (1H, dd, J=13.5, 5 Hz), 10 3.09 (1H, m), 3.19 (1H, dd, J=13.5, 10 Hz), 3.22 (1H, dd, J=14, 8 Hz), 3.94 (1H, m), 4.18 (1H, q, J=7 Hz), 4.24 (1H, m), 4.61 (1H, dd, J=8, 2 Hz), 4.74 (1H, ddd, J=10, 8, 7 Hz), 5.06 (1H, ddd, J=10.5, 10, 5 Hz), 6.35 (1H, d, J=10 Hz), 6.49 (1H, d, J=10.5 Hz), 7.12 (1H, d, J=10.5 Hz), 7.12-7.32 (10H, m), 7.32-7.48 (6H, m), 7.58-7.68 (4H, m);

15 MASS (ES+): m/e 829.

#### Example 304

Compound E304 was obtained from the Compound E303 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 1.18-1.34 (4H, m), 1.38 (3H, d, J=7.3 Hz), 20 1.52-1.87 (6H, m), 2.12-2.55 (4H, m), 2.85 (1H, dd, J=14, 7.5 Hz), 2.87 (1H, dd, J=13.5, 5 Hz), 3.08 (1H, m), 3.18 (1H, dd, J=13.5, 10.5 Hz), 3.21 (1H, dd, J=14, 8 Hz), 3.56 (1H, d, J=4.8 Hz), 3.94 (1H, m), 4.17-4.30 (2H, m), 4.62 (1H, dd, J=8, 2.5 Hz), 4.74 (1H, ddd, J=10, 8, 7.5 Hz), 5.06 (1H, ddd, J=10.5, 10.5, 5 Hz), 6.40 (1H, d, J=10 Hz), 25 7.12-7.32 (11H, m);

MASS (ES+): m/e 591.

#### Example 305

Compound E305 was obtained from the Compound (550) in a manner similar to Example 1.

30 <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.74 (3H, m), 0.79 (3H, d, J=6 Hz), 1.19-1.97 (12H, m), 1.23 (3H, d, J=7 Hz), 2.23 (2H, m), 2.46 (1H, m), 2.69 (1H, m), 2.88 (1H, dd, J=14, 6 Hz), 3.25 (1H, dd, J=14, 9 Hz), 4.27 (1H, q, J=7 Hz), 4.43-4.70 (4H, m), 4.81 (1H, m), 5.81-5.95 (2H, br), 6.16 (1H, d, J=10 Hz), 6.61 (1H, d, J=16 Hz), 6.85 (1H, dt, J=16, 7 35 Hz), 7.15-7.29 (5H, m), 7.30-7.48 (6H, m), 7.56-7.69 (4H, m);

MASS (ES+): m/e 807.51.

Example 306

Compound E306 was obtained from the Compound E305 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.73 (3H, m), 0.78 (3H, d, J=6.5 Hz), 1.10 (3x3H, s), 1.16-1.94 (16H, m), 1.18 (3H, d, J=6.8 Hz), 2.40-2.53 (3H, m), 2.70 (1H, m), 2.87 (1H, dd, J=13.8, 6.3 Hz), 3.25 (1H, dd, J=13.8, 9.8 Hz), 4.19 (1H, q, J=6.8 Hz), 4.40-4.69 (4H, m), 4.80 (1H, m), 5.82-5.93 (2H, m), 6.17 (1H, d, J=11 Hz), 7.15-7.28 (5H, m), 7.32-7.48 (6H, m), 7.58-7.68 (4H, m);  
MASS (ES<sup>+</sup>): m/e 809.60.

Example 307

Compound E307 was obtained from the Compound E306 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.72 (3H, m), 0.78 (3H, d, J=7 Hz), 1.09 (1H, m), 1.18-1.94 (15H, m), 1.38 (3H, d, J=7.3 Hz), 2.34-2.58 (3H, m), 2.72 (1H, m), 2.88 (1H, dd, J=13.5, 6.3 Hz), 3.25 (1H, dd, J=13.5, 9.5 Hz), 3.56 (1H, d, J=4 Hz), 4.23 (1H, m), 4.44-4.70 (4H, m), 4.84 (1H, m), 5.98-6.11 (2H, br), 6.24 (1H, d, J=11 Hz), 7.14-7.29 (5H, m);  
MASS (ES<sup>+</sup>): m/e 571.60.

Example 308

Compound E308 was obtained from the Compound (78) in a manner similar to Example 1.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.09 (3x3H, s), 1.22 (3H, d, J=7 Hz), 1.28 (3H, s), 1.38-1.53 (2H, m), 1.61 (1H, m), 1.71-1.91 (3H, m), 2.09-2.40 (6H, m), 2.90 (1H, dd, J=13.5, 5.5 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.86 (1H, m), 4.21 (1H, m), 4.27 (1H, q, J=7 Hz), 4.67 (1H, m), 5.03 (2H, s), 5.14 (1H, ddd, J=10, 9.5, 5.5 Hz), 5.80 (1H, s), 6.62 (1H, d, J=16 Hz), 6.87 (1H, m), 6.89 (2x1H, d, J=8.8 Hz), 7.13 (1H, d, J=10 Hz), 7.14 (2x1H, d, J=8.8 Hz), 7.30-7.48 (11H, m), 7.50 (1H, d, J=10 Hz), 7.56-7.70 (4H, m);  
MASS (ES<sup>+</sup>): m/e 885.20.

Example 309

Compound E309 was obtained from the Compound E308 in a manner similar to Example 3.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.83 (3H, t, J=7.3 Hz), 1.10 (3x3H, s), 1.16-1.36 (4H, m), 1.18 (3H, d, J=7 Hz), 1.28 (3H, s), 1.40-1.52 (2H,

m), 1.61 (1H, m), 1.70-1.89 (3H, m), 2.06-2.40 (4H, m), 2.51 (2H, m), 2.89 (1H, dd, J=13.5, 5.5 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.85 (1H, m), 4.18 (1H, q, J=7 Hz), 4.18 (1H, m), 4.67 (1H, m), 5.03 (2H, s), 5.13 (1H, ddd, J=10, 10, 5.5 Hz), 5.81 (1H, s), 6.89 (2x1H, d, J=8.5 Hz), 7.08 (1H, d, J=10.3 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.30-7.49 (11H, m), 7.55 (1H, d, J=10 Hz), 7.59-7.70 (4H, m);  
MASS (ES+): m/e 887.31.

#### Example 310

Compound E310 was obtained from the Compound E309 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 1.24-1.44 (4H, m), 1.28 (3H, s), 1.38 (3H, d, J=7 Hz), 1.54-1.70 (3H, m), 1.71-1.90 (3H, m), 2.07-2.58 (6H, m), 2.89 (1H, dd, J=13.5, 6.5 Hz), 3.18 (1H, dd, J=13.5, 10 Hz), 3.26 (1H, m), 3.55 (1H, d, J=4.5 Hz), 3.86 (1H, m), 4.14-4.28 (2H, m), 4.67 (1H, m), 5.03 (1H, s), 5.13 (1H, ddd, J=10, 10, 6.5 Hz), 5.79 (1H, s), 6.89 (2x1H, d, J=8.5 Hz), 7.11 (1H, d, J=10 Hz), 7.15 (2x1H, d, J=8.5 Hz), 7.25-7.47 (5H, m), 7.52 (1H, d, J=10 Hz);  
MASS (ES+): m/e 649.36.

#### Example 311

The Compound E9 (320 mg) was dissolved in tetrahydrofuran (4 ml). Cold hydrogen fluoride-pyridine (1 ml) was added to the mixture and the mixture was stirred at ambient temperature for about 3 hours. The reaction mixture was neutralized with saturated aqueous sodium hydrogen bicarbonate and then with 1N aqueous sodium hydroxide. The mixture was extracted with ethyl acetate. The ethyl acetate layer was washed with saturated brine and dried over sodium sulfate, and the solvent was removed by evaporation. The residue was purified by thin layer chromatography (eluting with ethyl acetate) and lyophilized from t-butanol to give the objective Compound E311 as a white amorphous.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.85 (3H, t, J=7.5 Hz), 1.29 (3H, s), 1.38 (3H, d, J=7 Hz), 1.42-1.92 (6H, m), 2.08-2.41 (6H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.65 (1H, d, J=5 Hz), 3.77 (1H, s), 3.86 (1H, m), 4.22 (1H, dt, J=10, 7.5 Hz), 4.44 (1H, dq, J=7.5, 5 Hz), 4.67 (1H, m), 5.14 (1H, ddd, J=10, 9.5, 6 Hz), 5.90 (1H, s), 6.25 (1H, brd, J=16 Hz), 6.81 (2x1H, d, J=8.5 Hz), 7.01 (1H, dt, J=16, 7 Hz), 7.14 (2x1H, d, J=8.5 Hz), 7.18 (1H, d, J=10

Hz), 7.48 (1H, d, J=10 Hz);

MASS (ES+): m/e 571.35;

$[\alpha]_D^{30} = -104.1^\circ$  (c=0.32, CHCl<sub>3</sub>).

Example 312

5 Compound E312 was obtained from the Compound E26 in a manner similar to Preparation 78.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.3 Hz), 1.22-1.42 (4H, m), 1.28 (3H, s), 1.39 (3H, t, J=7 Hz), 1.51-1.89 (6H, m), 2.07-2.38 (4H, m), 2.34 (3H, s), 2.73 (2H, t, J=7.3 Hz), 2.88 (1H, dd, J=13.5, 6 Hz),  
10 3.17 (1H, dd, J=13.5, 10 Hz), 3.25 (1H, m), 3.85 (1H, m), 3.99 (2H, q, J=7 Hz) 4.19 (1H, dt, J=10, 7.5 Hz), 4.66 (1H, m), 5.13 (1H, ddd, J=10, 10, 6 Hz), 5.80 (1H, s), 6.80 (2x1H, d, J=8.5 Hz), 7.09 (1H, d, J=10 Hz), 7.13 (2x1H, d, J=8.5 Hz), 7.52 (1H, d, J=10 Hz);

MASS (ES+): m/e 585.45;

15  $[\alpha]_D^{22} = -111.3^\circ$  (c=0.23, CHCl<sub>3</sub>).

Example 313

Compound E313 was obtained from the Compound E5 in a manner similar to Preparation (387).

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.2 Hz), 1.10 (3x3H, s),  
20 1.16-1.32 (4H, m), 1.18 (3H, d, J=7 Hz), 1.28 (3H, s), 1.38-1.62 (3H, m), 1.70-1.86 (3H, m), 2.08-2.39 (4H, m), 2.51 (2H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.85 (1H, m), 4.12-4.24 (2H, m), 4.49 (2H, ddd, J=5, 1.5, 1.5 Hz), 4.67 (1H, m), 5.13 (1H, ddd, J=10.3, 9.5, 6 Hz), 5.27 (1H, ddt, J=10.3, 1.5, 1.5 Hz),  
25 5.40 (1H, ddt, J=17.2, 1.5, 1.5 Hz), 5.83 (1H, s), 6.04 (1H, ddt, J=17.2, 10.3, 5 Hz), 6.82 (2x1H, d, J=8.6 Hz), 7.08 (1H, d, J=10.2 Hz), 7.14 (2x1H, d, J=8.6 Hz), 7.32-7.48 (6H, m), 7.55 (1H, d, J=10.3 Hz), 7.58-7.67 (4H, m);

MASS (ES+): m/e 837.50.

30 Example 314

Compound E314 was obtained from the Compound E313 in a manner similar to Example 6.

<sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, δ): 0.84 (3H, t, J=7.5 Hz), 1.20-1.41 (4H, m), 1.29 (3H, s), 1.38 (3H, d, J=7 Hz), 1.52-1.70 (3H, m), 1.71-1.89 (3H, m), 2.07-2.58 (6H, m), 2.89 (1H, dd, J=13.5, 6 Hz), 3.18 (1H, dd, J=13.5, 9.5 Hz), 3.26 (1H, m), 3.55 (1H, d, J=4.5 Hz), 3.85 (1H, m),

4.13-4.29 (2H, m), 4.50 (2H, d, J=5.5 Hz), 4.67 (1H, dd, J=8, 2 Hz),  
5.13 (1H, ddd, J=10, 9.5, 6 Hz), 5.27 (1H, dd, J=10, 1.5 Hz), 5.40 (1H,  
dd, J=17, 1.5 Hz), 5.84 (1H, s), 6.04 (1H, ddt, J=17, 10, 5.5 Hz),  
6.83 (2x1H, d, J=8.5 Hz), 7.11 (1H, d, J=10 Hz), 7.13 (2x1H, d, J=8.5  
5 Hz), 7.52 (1H, d, J=10 Hz);  
MASS (ES+): m/e 599.53;  
[ $\alpha$ ]<sub>D</sub><sup>25</sup> = -110.4° (c=0.24, CHCl<sub>3</sub>).

The compounds obtained in the above-mentioned Preparations and  
10 Examples are listed in the following Tables 2-1 to 2-109.

Table 2

Table 2-1

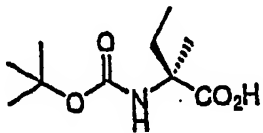
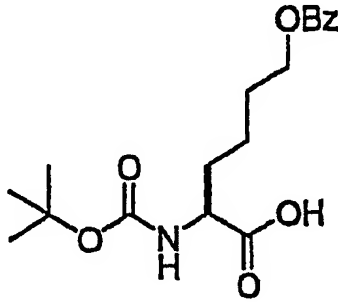
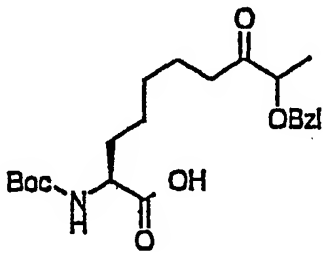
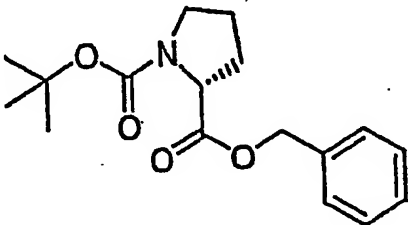
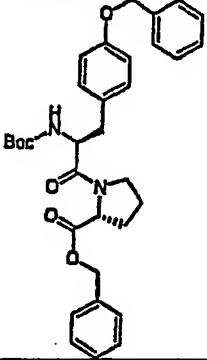
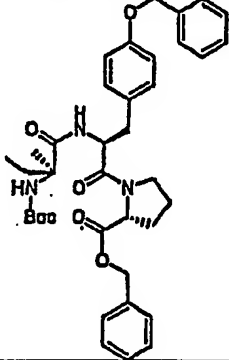
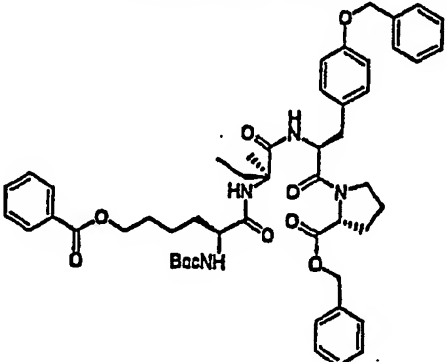
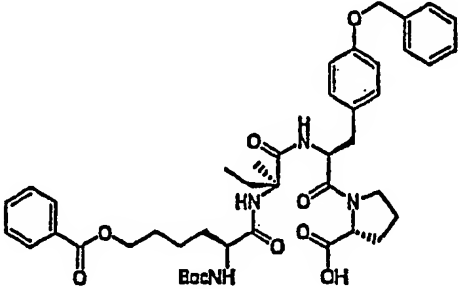
Compound (1)	Compound (5)
	
Compound (12)	Compound (13)
	
Compound (14)	Compound (15)
	
Compound (16)	Compound (17)
	

Table 2-2

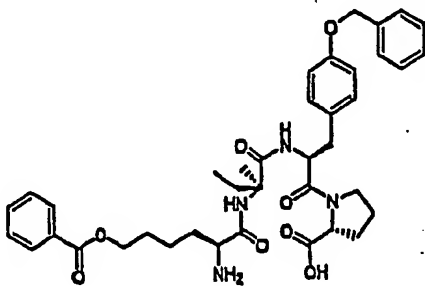
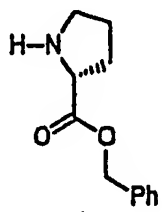
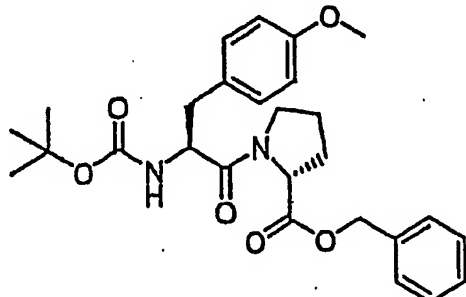
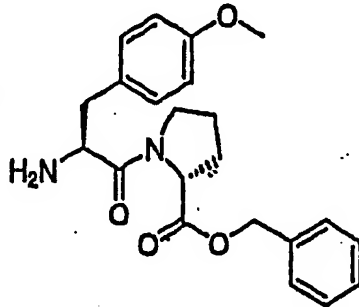
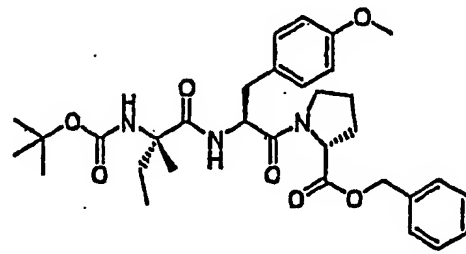
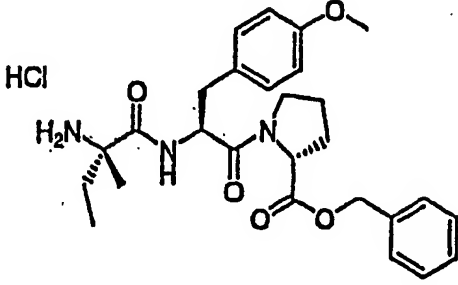
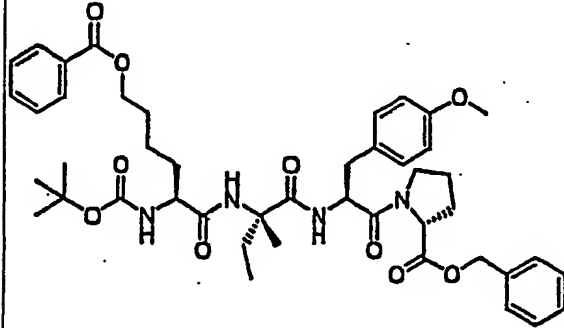
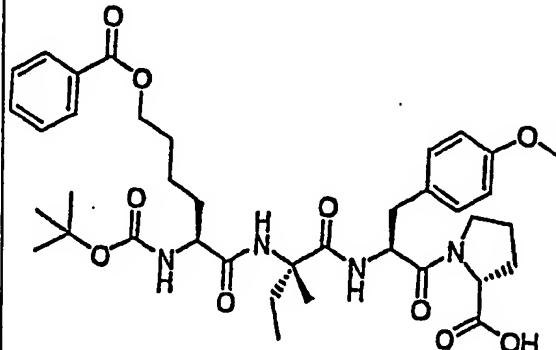
Compound (18)	Compound (19)
 <p>HCl</p>	 <p>HCl</p>
Compound (20)	Compound (21)
	 <p>HCl</p>
Compound (22)	Compound (23)
	 <p>HCl</p>
Compound (24)	Compound (25)
	

Table 2-3

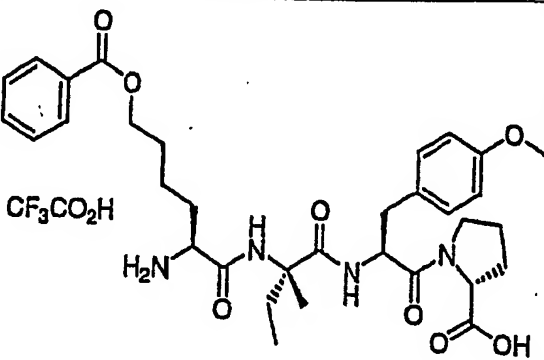
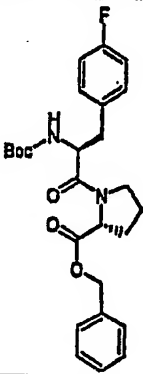
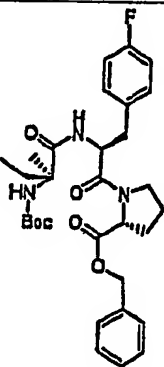
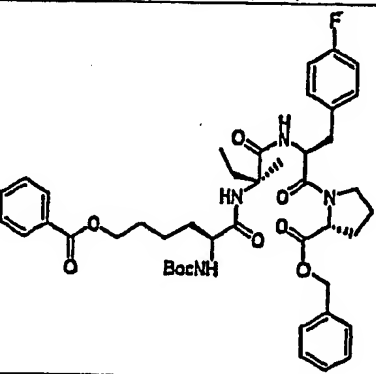
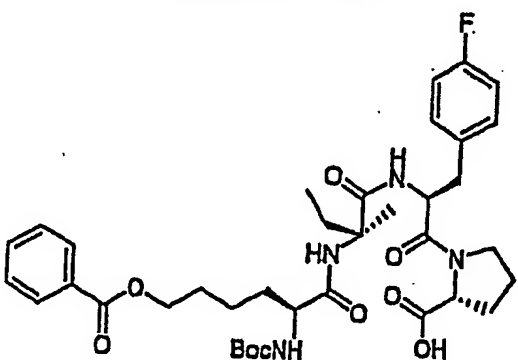
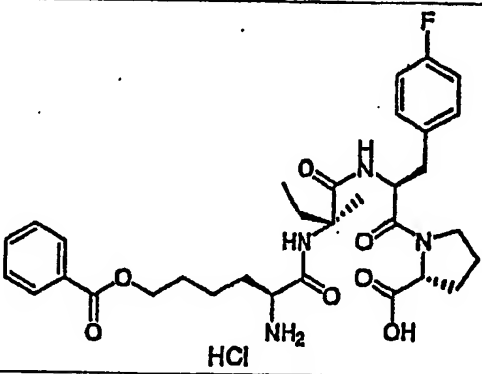
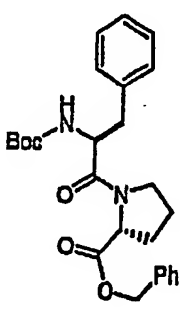
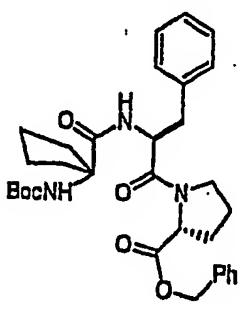
Compound (26)	Compound (27)
	
Compound (28)	Compound (29)
	
Compound (30)	Compound (31)
	
Compound (32)	Compound (33)
	

Table 2-4

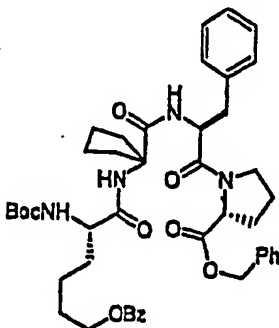
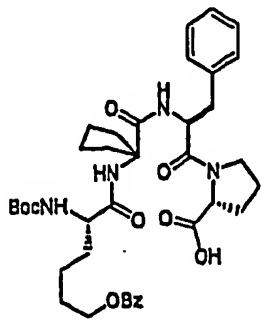
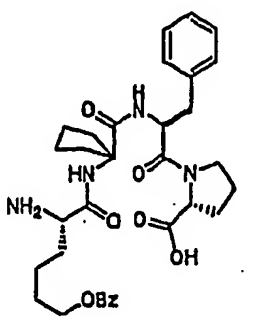
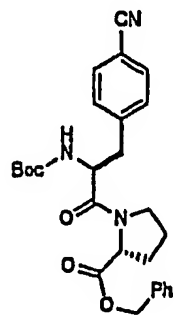
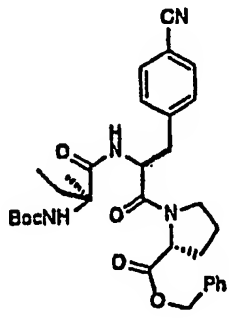
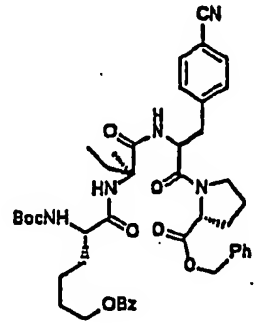
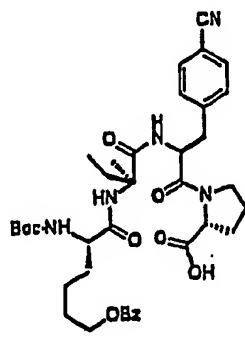
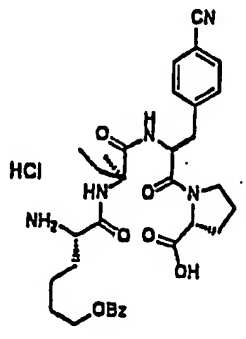
Compound (34)	Compound (35)
	
Compound (36)	Compound (37)
 HCl	
Compound (38)	Compound (39)
	
Compound (40)	Compound (41)
	 HCl

Table 2-5

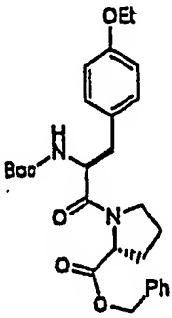
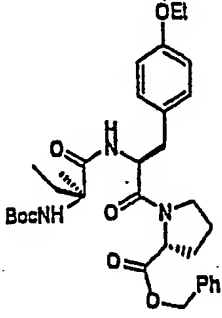
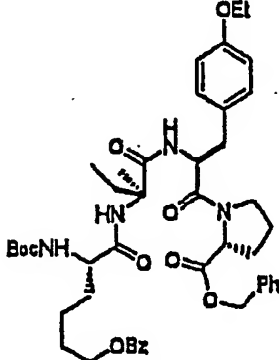
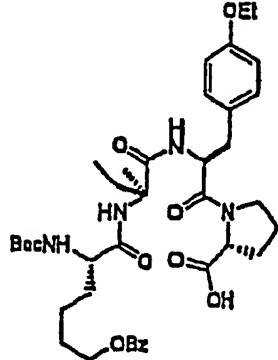
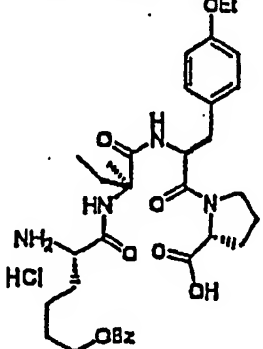
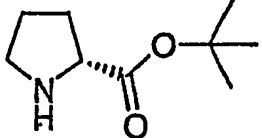
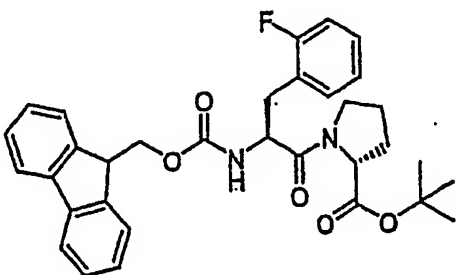
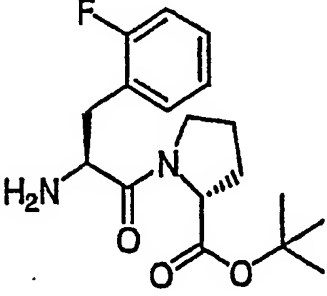
Compound (42)	Compound (43)
	
Compound (44)	Compound (45)
	
Compound (46)	Compound (47)
	
Compound (48)	Compound (49)
	

Table 2-6

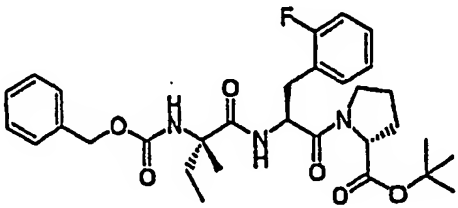
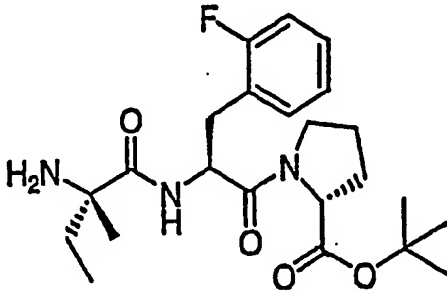
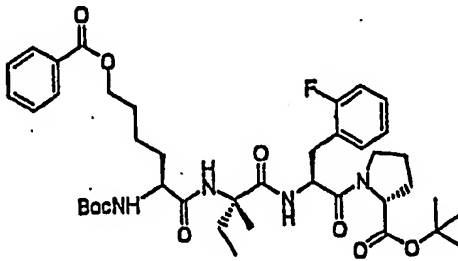
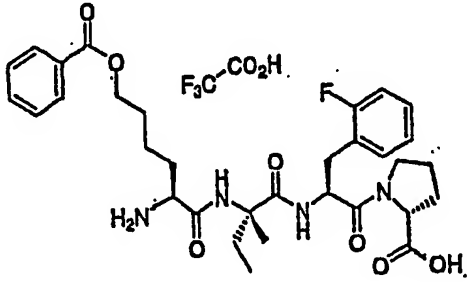
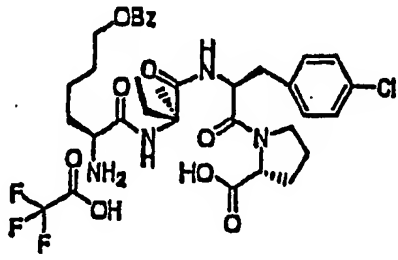
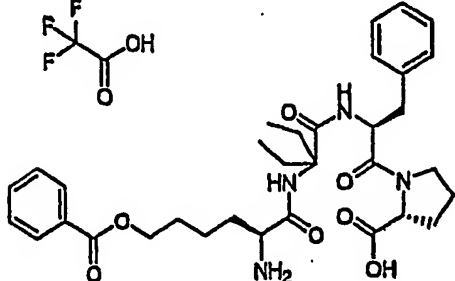
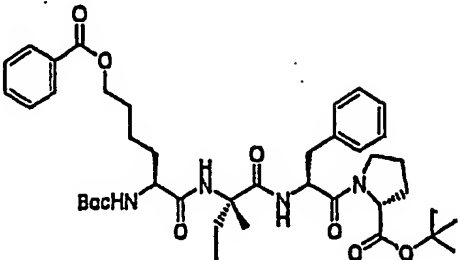
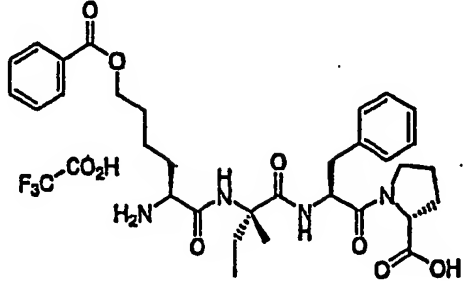
Compound (50)	Compound (51)
	
Compound (52)	Compound (53)
	
Compound (54)	Compound (55)
	
Compound (56)	Compound (57)
	

Table 2-7

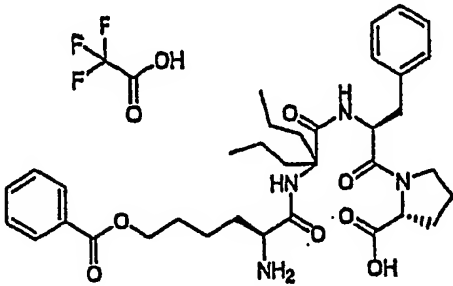
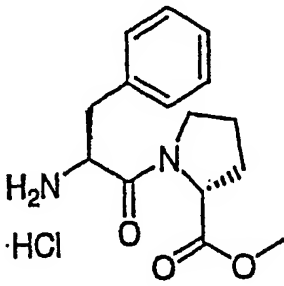
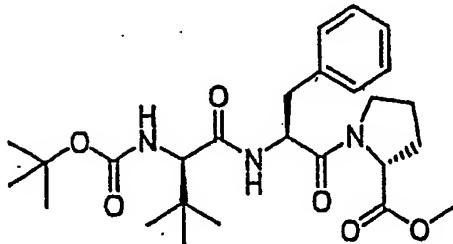
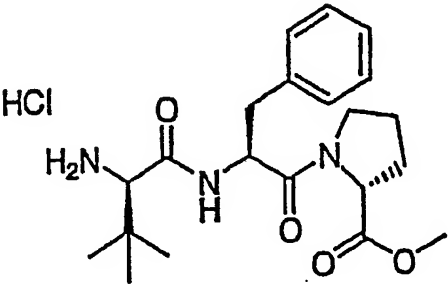
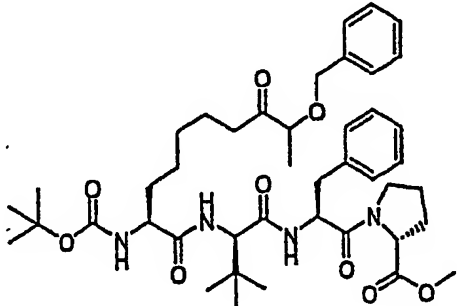
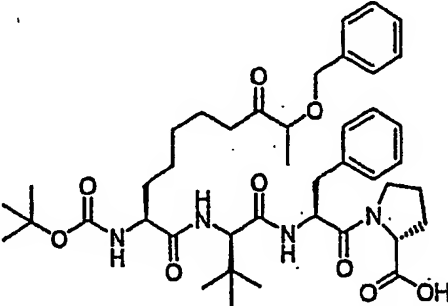
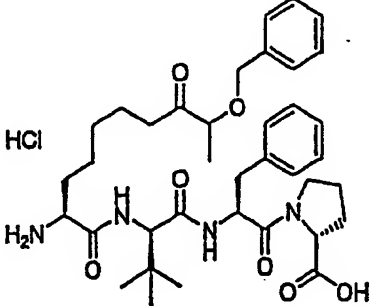
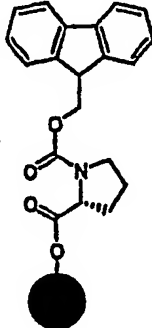
Compound (58)	Compound (59)
	
Compound (60)	Compound (61)
	
Compound (62)	Compound (63)
	
Compound (64)	Compound (65)
	

Table 2-8

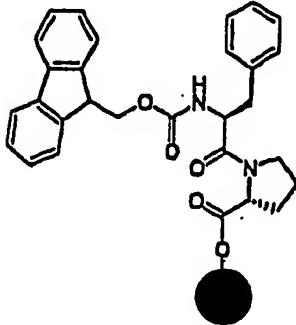
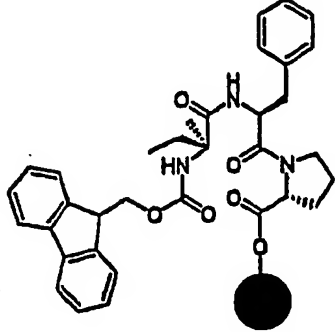
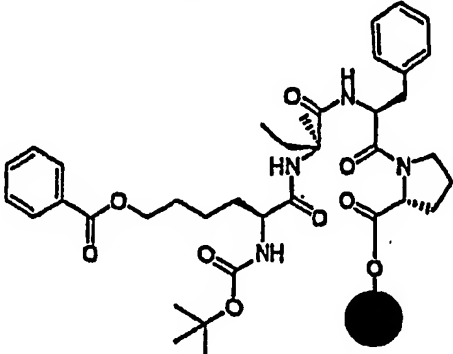
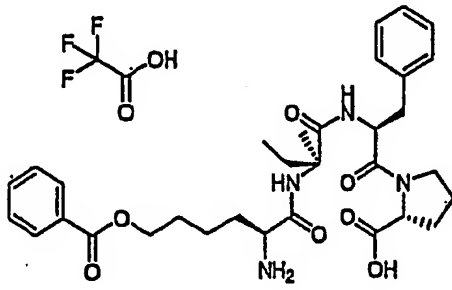
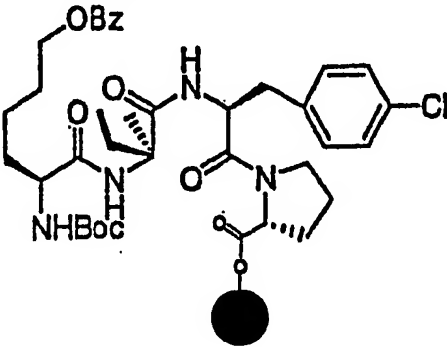
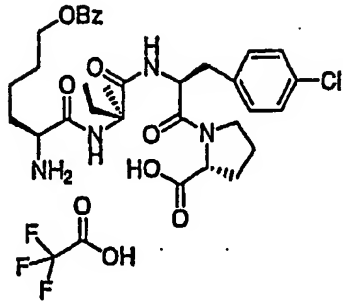
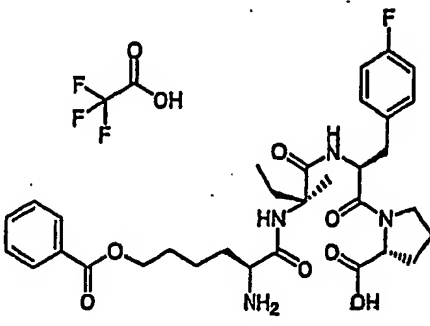
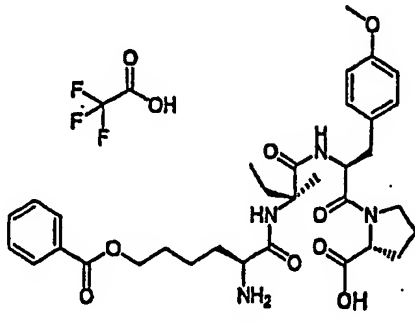
Compound (66)	Compound (67)
	
Compound (68)	Compound (69)
	
Compound (70)	Compound (71)
	
Compound (72)	Compound (73)
	

Table 2-9

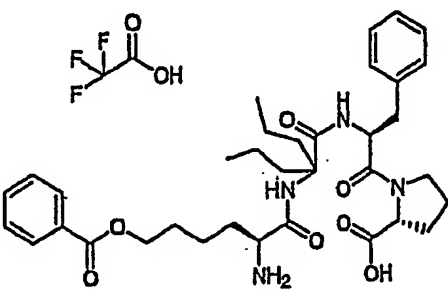
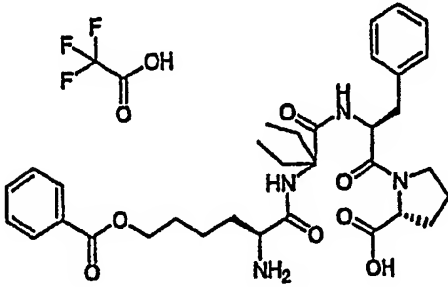
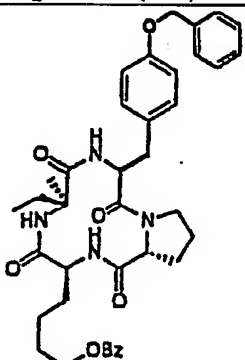
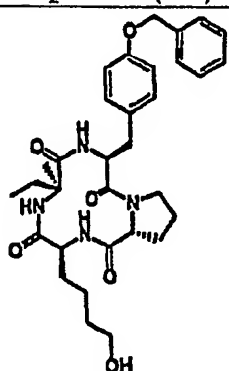
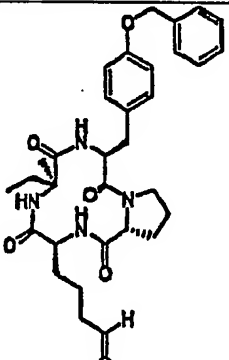
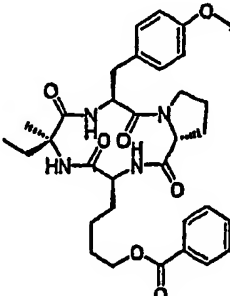
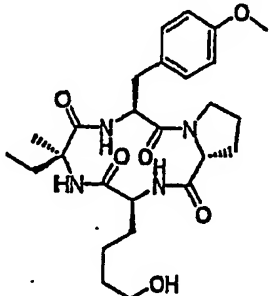
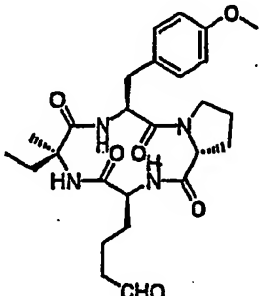
Compound (74)	Compound (75)
	
Compound (76)	Compound (77)
	
Compound (78)	Compound (79)
	
Compound (80)	Compound (81)
	

Table 2-10

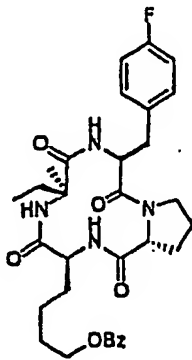
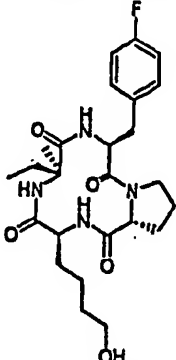
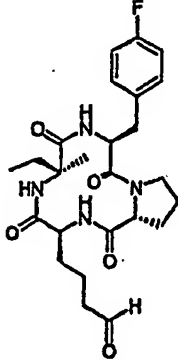
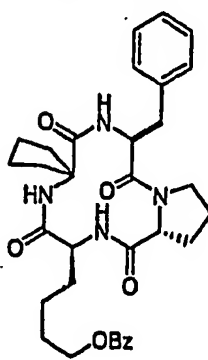
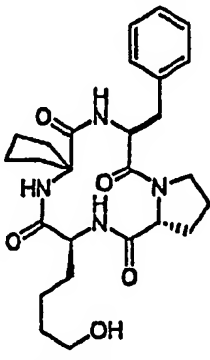
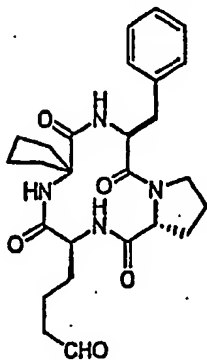
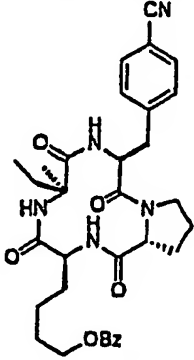
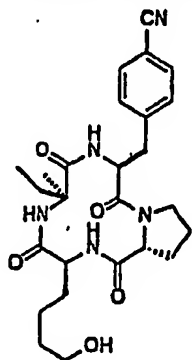
Compound (82)	Compound (83)
	
Compound (84)	Compound (85)
	
Compound (86)	Compound (87)
	
Compound (88)	Compound (89)
	

Table 2-11

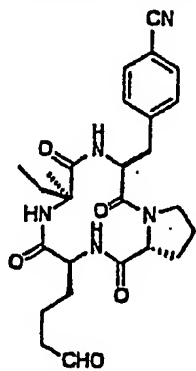
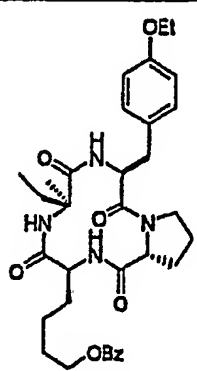
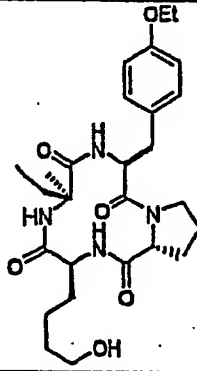
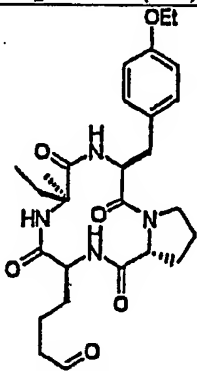
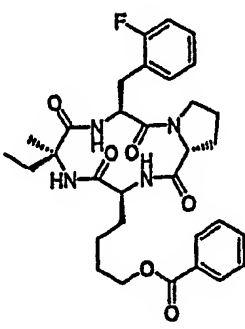
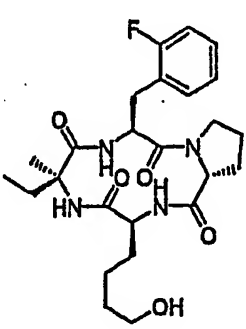
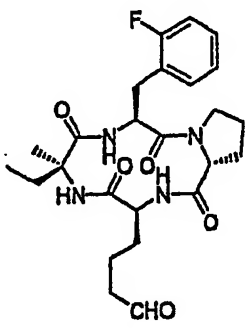
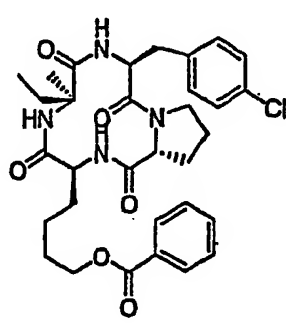
Compound (90)	Compound (91)
	
Compound (92)	Compound (93)
	
Compound (94)	Compound (95)
	
Compound (96)	Compound (97)
	

Table 2-12

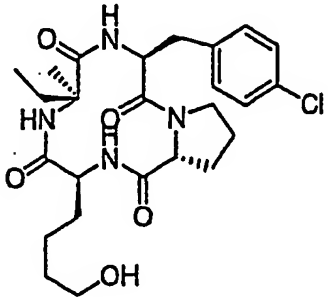
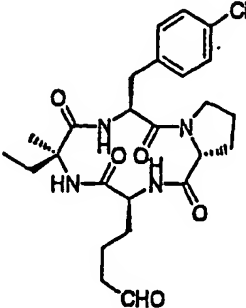
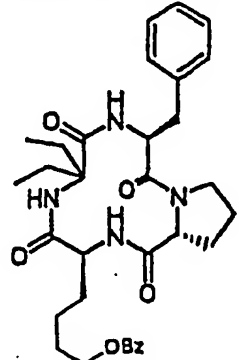
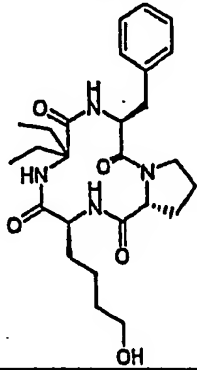
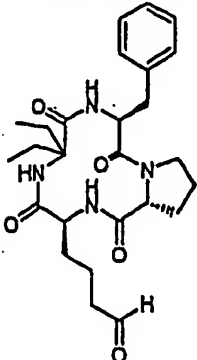
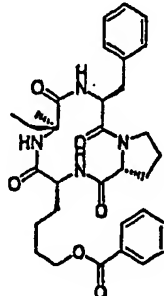
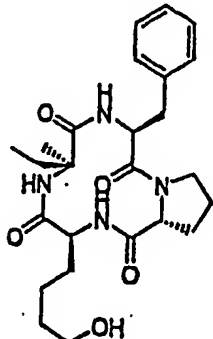
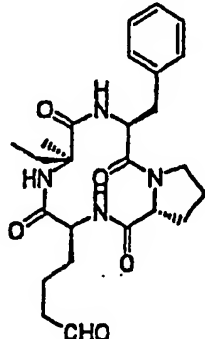
Compound (98)	Compound (99)
	
Compound (100)	Compound (101)
	
Compound (102)	Compound (103)
	
Compound (104)	Compound (105)
	

Table 2-13

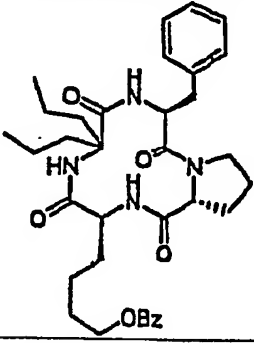
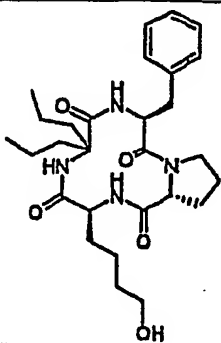
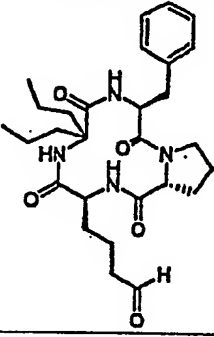
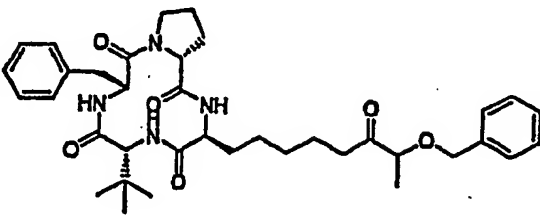
Compound (106)	Compound (107)
	
Compound (108)	Compound (109)
	

Table 2-14

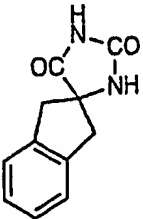
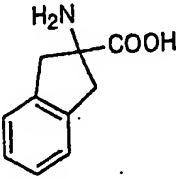
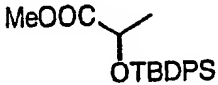
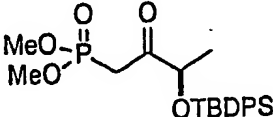
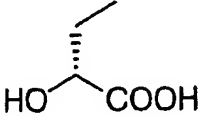
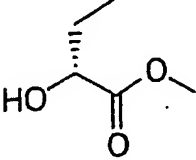
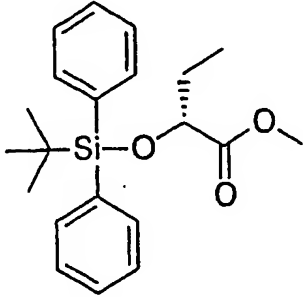
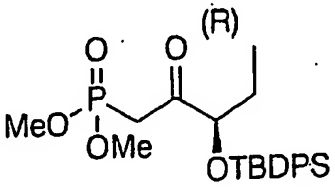
Compound (110)	Compound (111)
	
Compound (112)	Compound (113)
	
Compound (114)	Compound (115)
	
Compound (116)	Compound (117)
	

Table 2-15

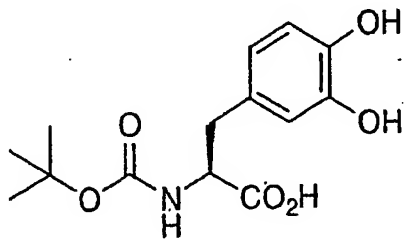
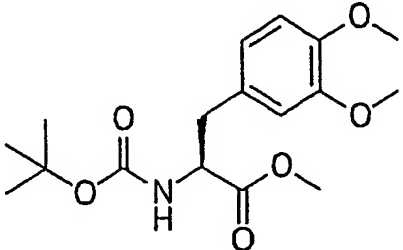
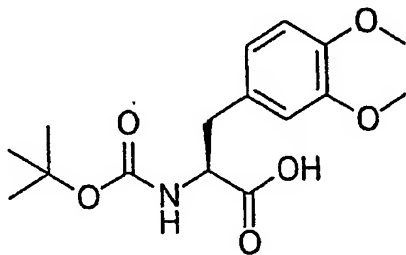
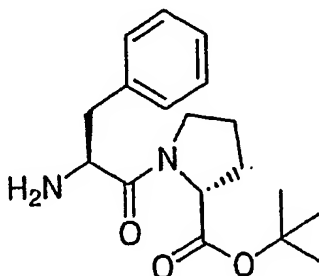
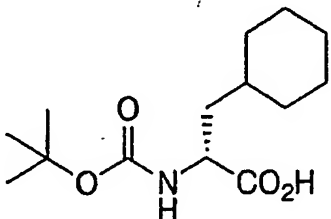
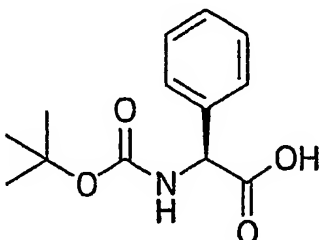
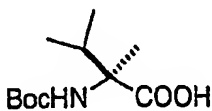
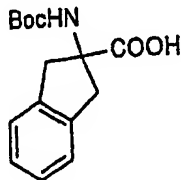
Compound (118)	Compound (119)
	
Compound (120)	Compound (121)
	
Compound (122)	Compound (123)
	
Compound (124)	Compound (125)
	

Table 2-16

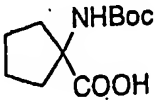
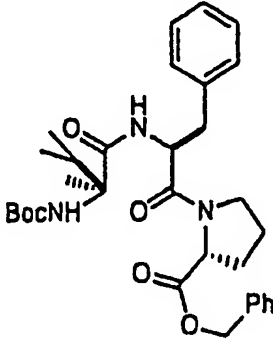
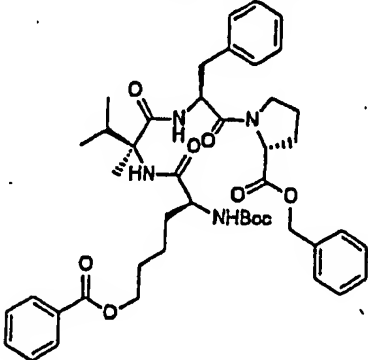
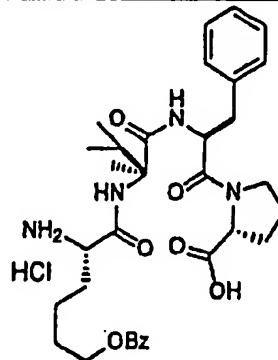
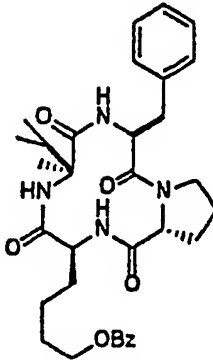
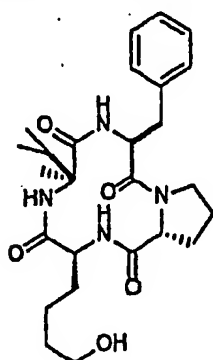
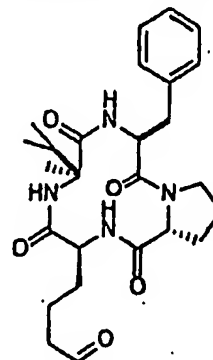
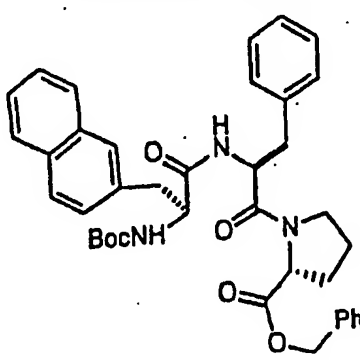
Compound (126)	Compound (127)
	
Compound (128)	Compound (129)
	
Compound (130)	Compound (131)
	
Compound (132)	Compound (133)
	

Table 2-17

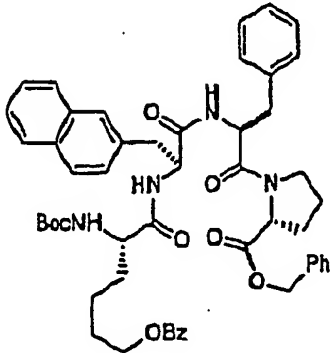
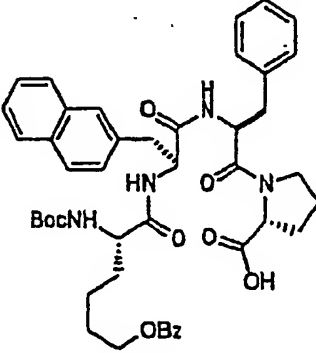
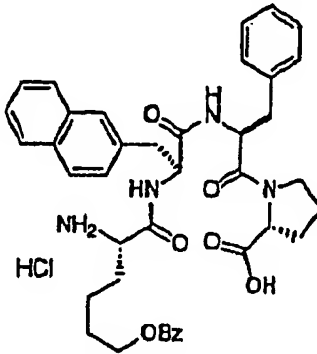
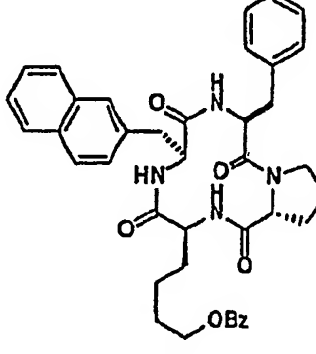
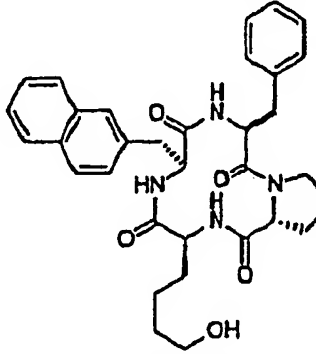
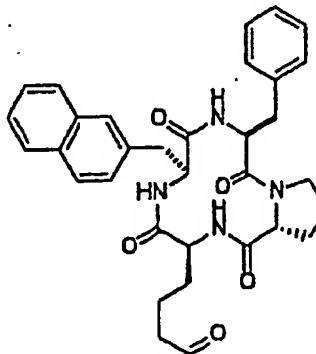
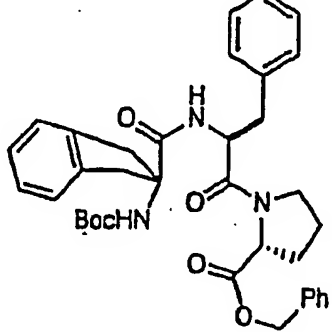
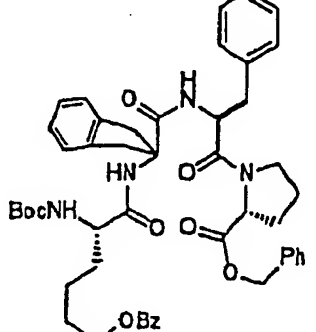
Compound (134)	Compound (135)
	
Compound (136)	Compound (137)
	
Compound (138)	Compound (139)
	
Compound (140)	Compound (141)
	

Table 2-18

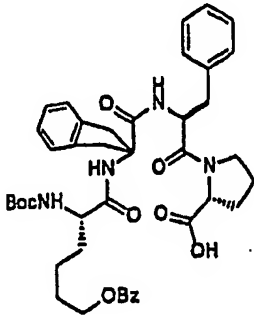
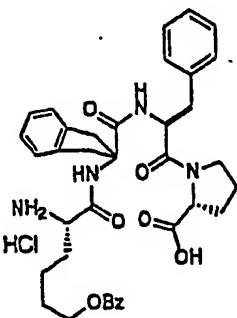
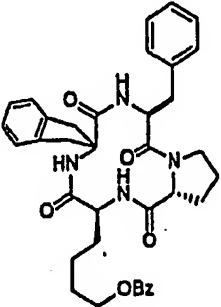
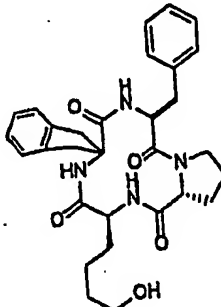
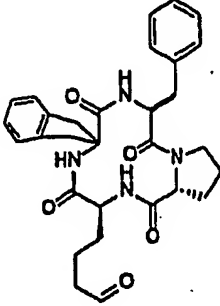
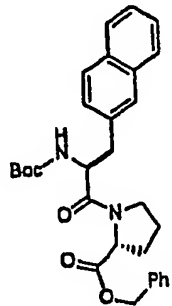
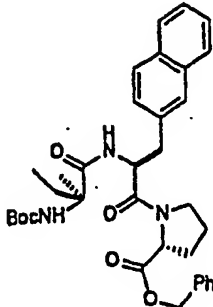
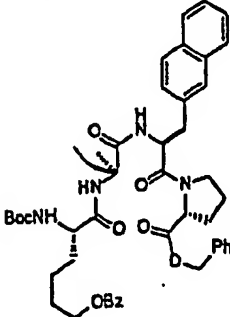
Compound (142)	Compound (143)
	
Compound (144)	Compound (145)
	
Compound (146)	Compound (147)
	
Compound (148)	Compound (149)
	

Table 2-19

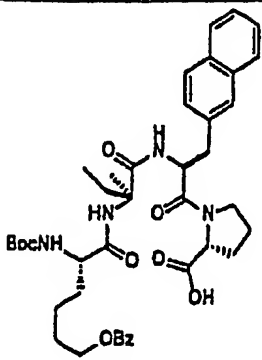
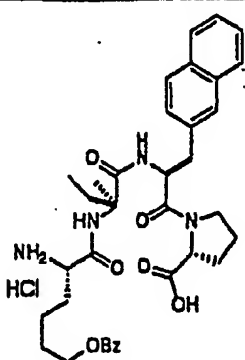
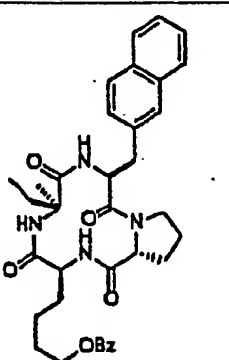
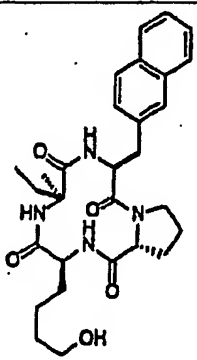
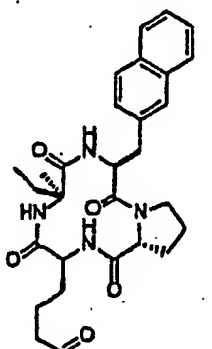
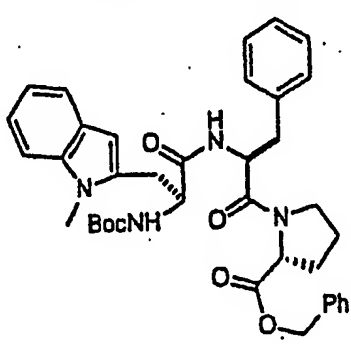
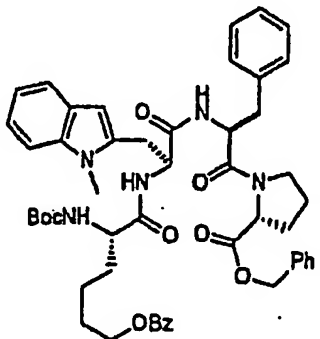
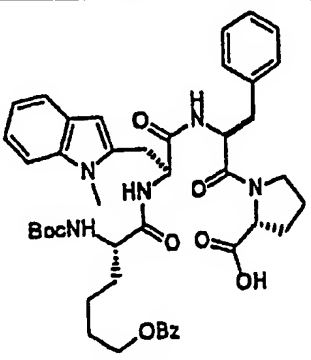
Compound (150)	Compound (151)
	
Compound (152)	Compound (153)
	
Compound (154)	Compound (155)
	
Compound (156)	Compound (157)
	

Table 2-20

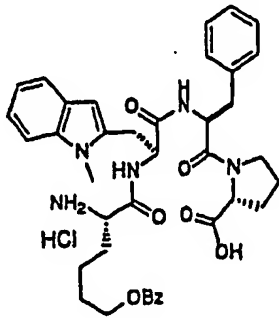
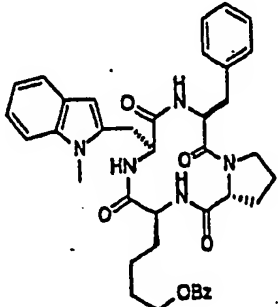
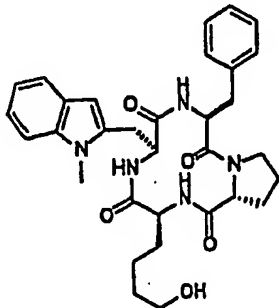
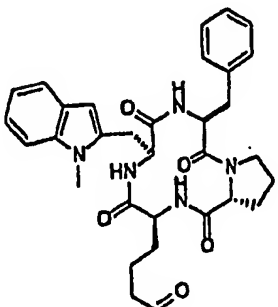
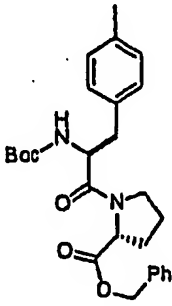
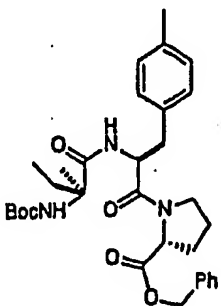
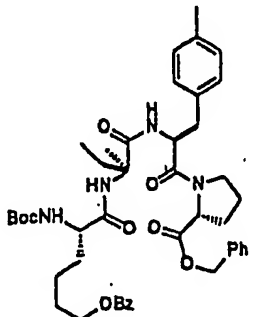
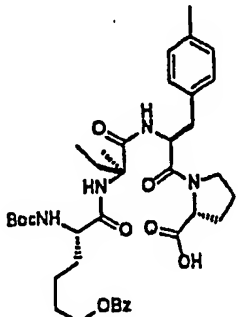
Compound (158)	Compound (159)
	
Compound (160)	Compound (161)
	
Compound (162)	Compound (163)
	
Compound (164)	Compound (165)
	

Table 2-21

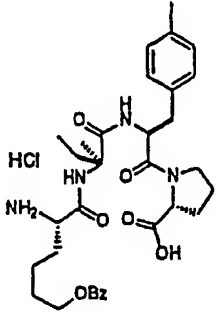
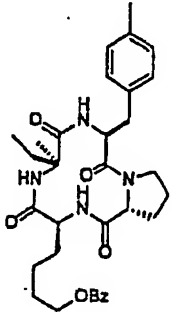
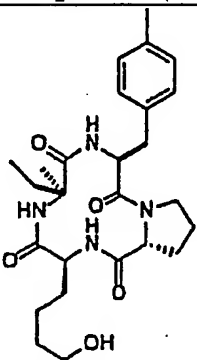
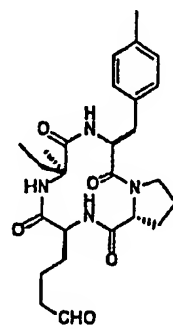
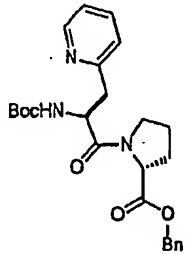
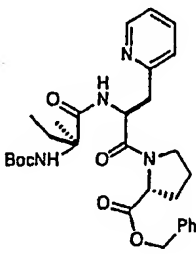
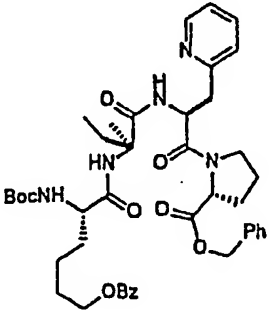
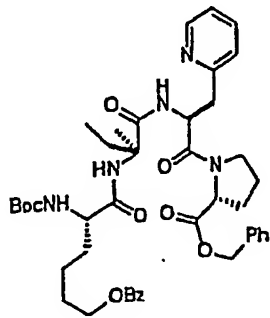
Compound (166)	Compound (167)
	
Compound (168)	Compound (169)
	
Compound (170)	Compound (171)
	
Compound (172)	Compound (173)
	

Table 2-22

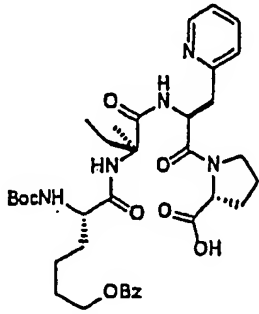
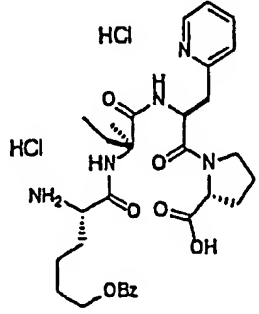
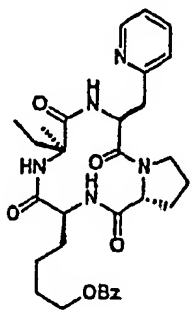
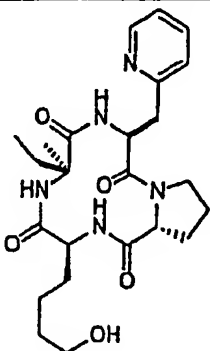
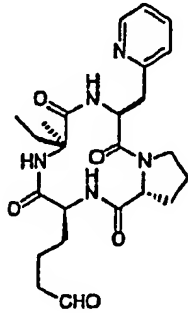
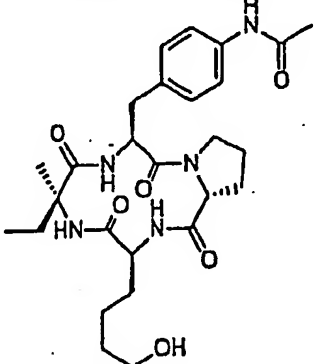
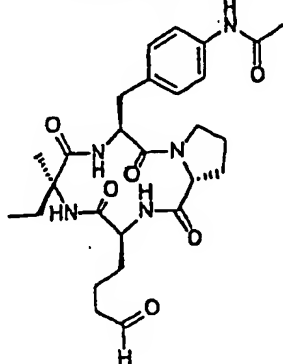
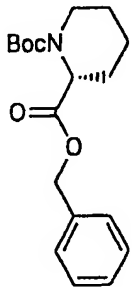
Compound (174)	Compound (175)
	
Compound (176)	Compound (177)
	
Compound (178)	Compound (179)
	
Compound (180)	Compound (181)
	

Table 2-23

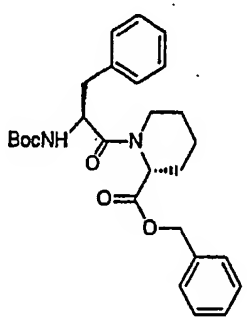
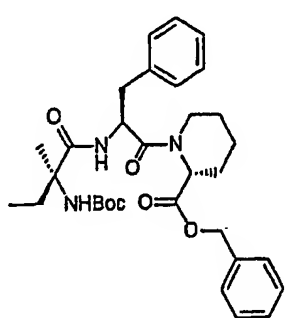
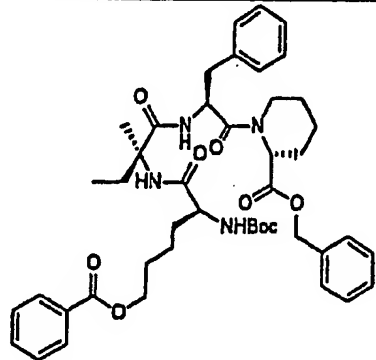
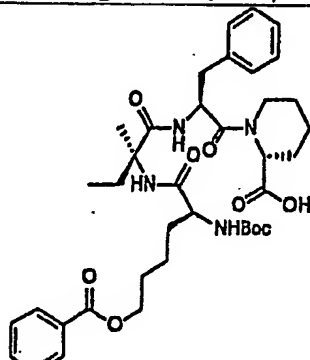
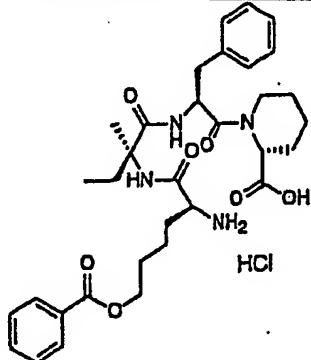
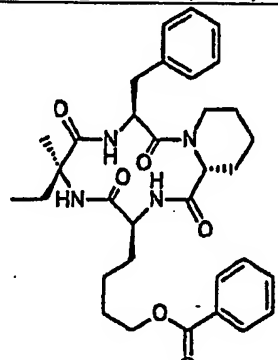
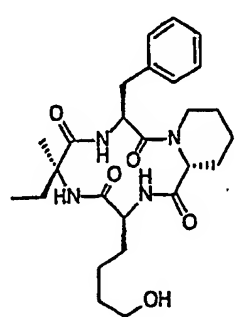
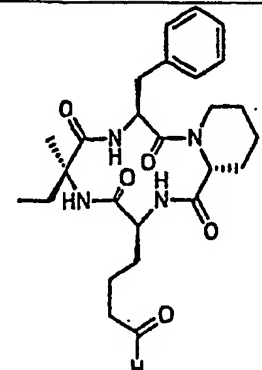
Compound (182)	Compound (183)
	
Compound (184)	Compound (185)
	
Compound (186)	Compound (187)
	
Compound (188)	Compound (189)
	

Table 2-24

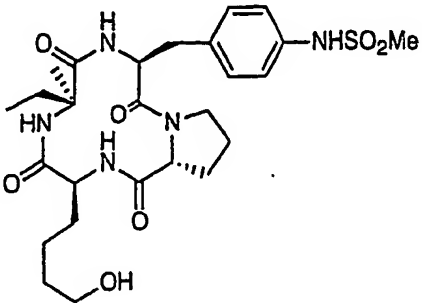
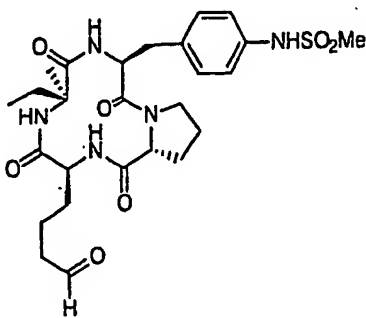
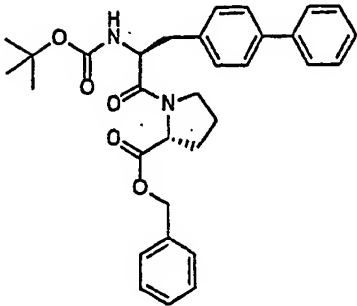
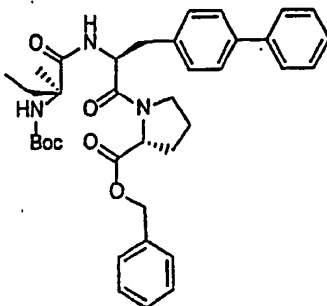
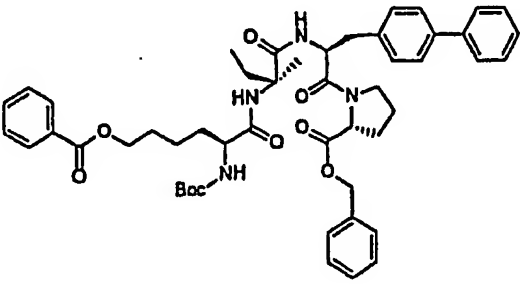
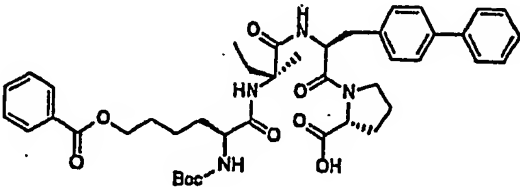
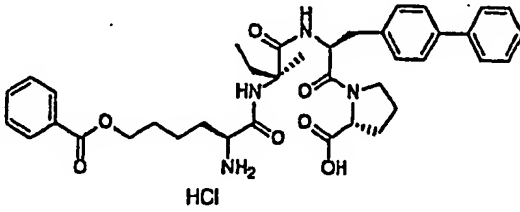
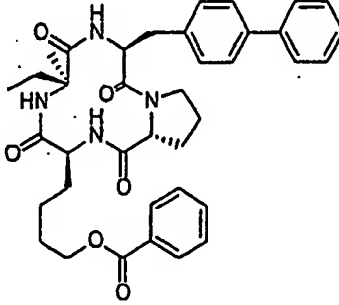
Compound (190)	Compound (191)
	
Compound (192)	Compound (193)
	
Compound (194)	Compound (195)
	
Compound (196)	Compound (197)
	

Table 2-25

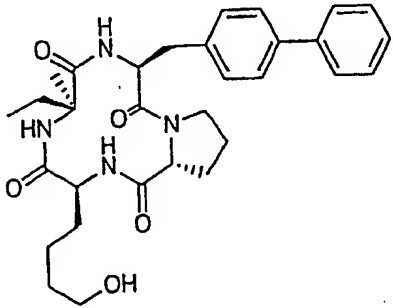
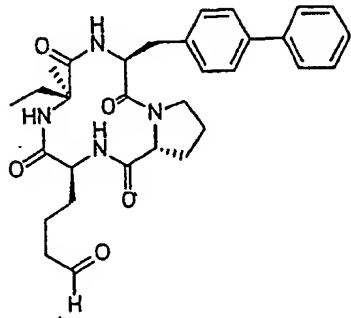
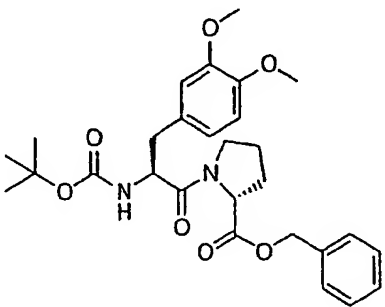
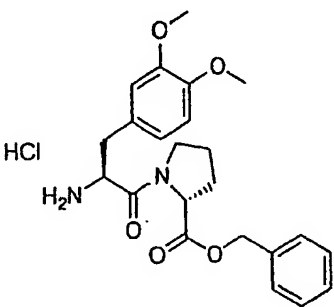
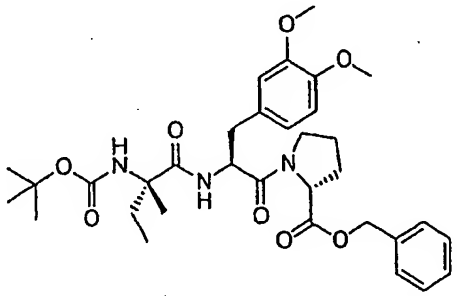
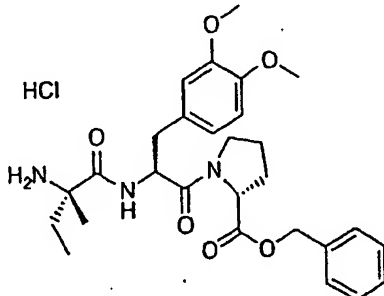
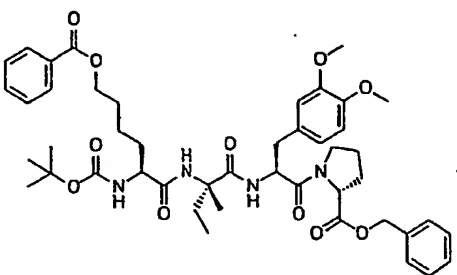
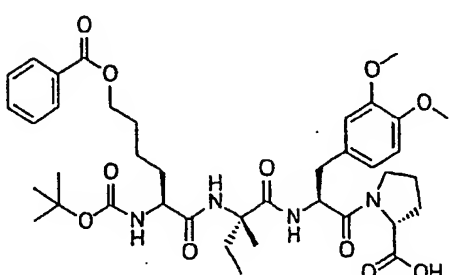
Compound (198)	Compound (199)
	
Compound (200)	Compound (201)
	
Compound (202)	Compound (203)
	
Compound (204)	Compound (205)
	

Table 2-26

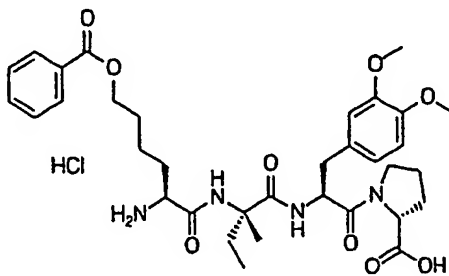
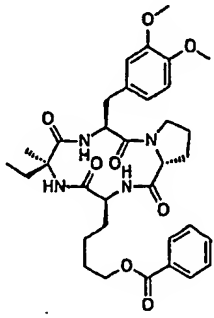
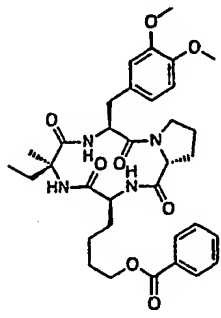
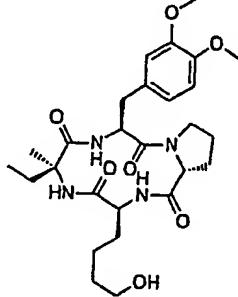
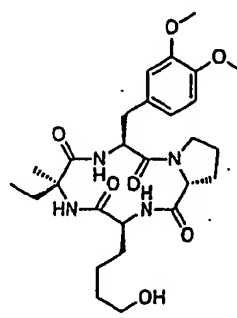
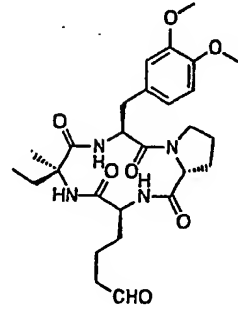
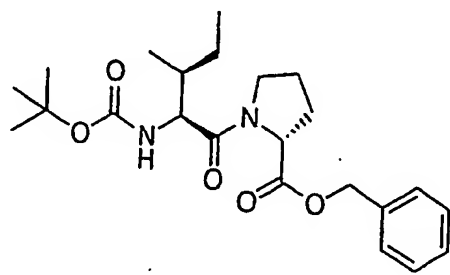
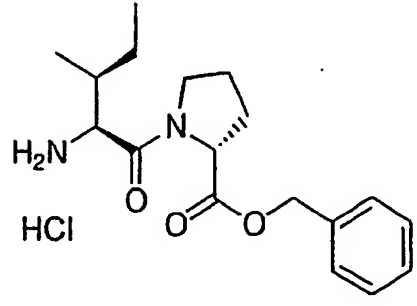
Compound (206)	Compound (207)
	
Compound (208)	Compound (209)
	
Compound (210)	Compound (211)
	
Compound (212)	Compound (213)
	

Table 2-27

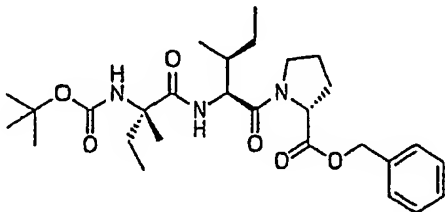
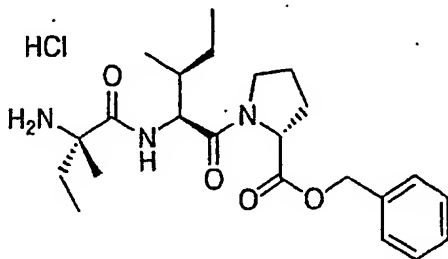
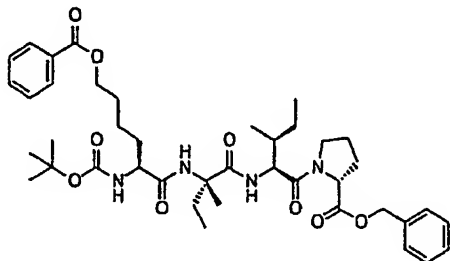
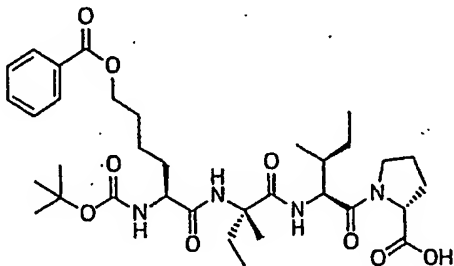
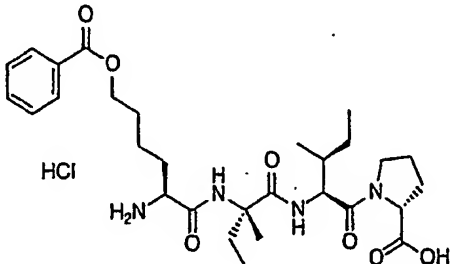
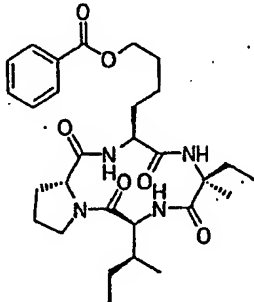
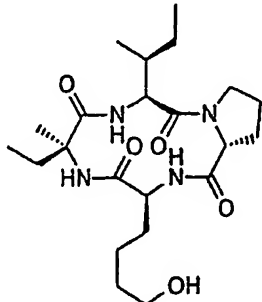
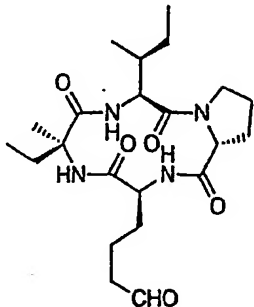
Compound (214)	Compound (215)
	
Compound (216)	Compound (217)
	
Compound (218)	Compound (219)
	
Compound (220)	Compound (221)
	

Table 2-28

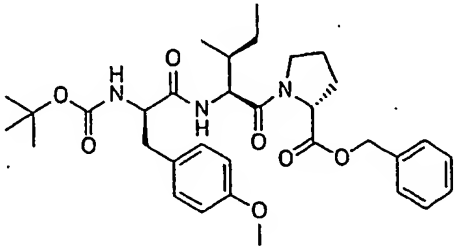
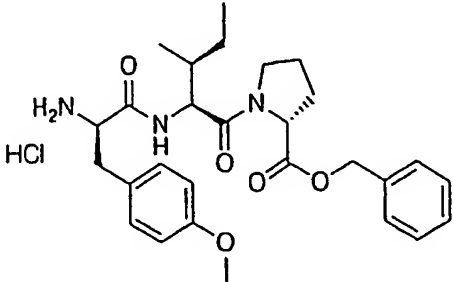
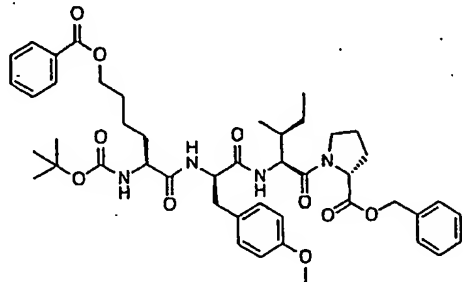
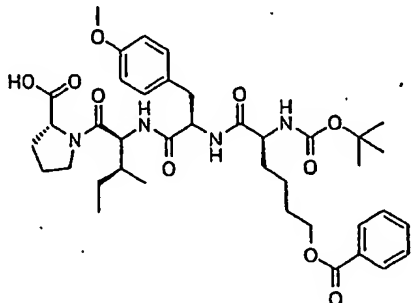
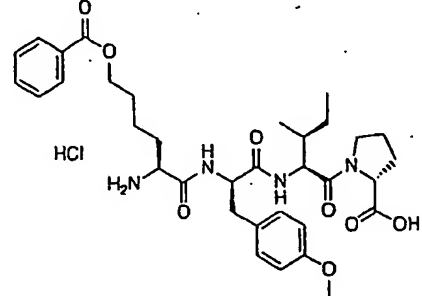
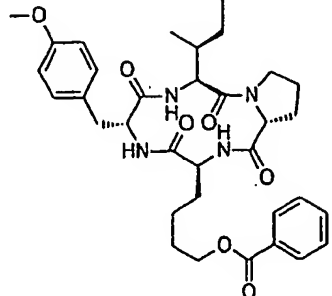
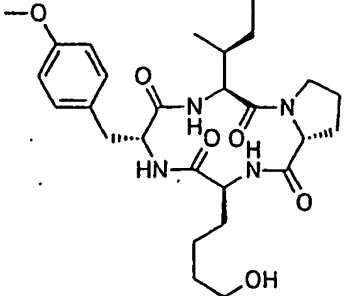
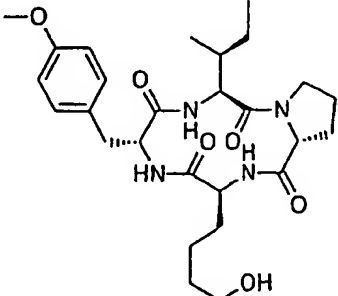
Compound (222)	Compound (223)
	
Compound (224)	Compound (225)
	
Compound (226)	Compound (227)
	
Compound (228)	Compound (229)
	

Table 2-29

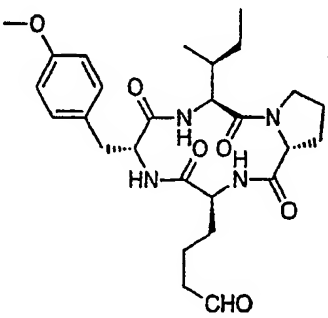
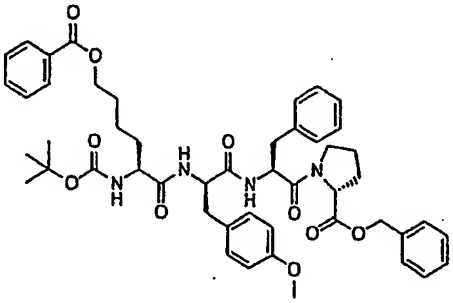
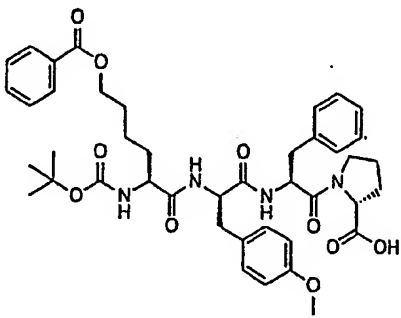
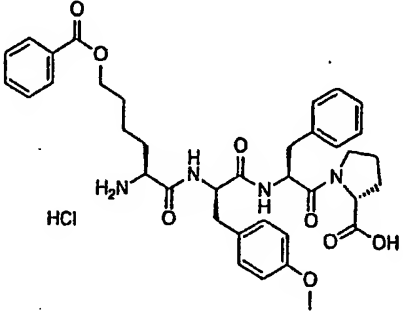
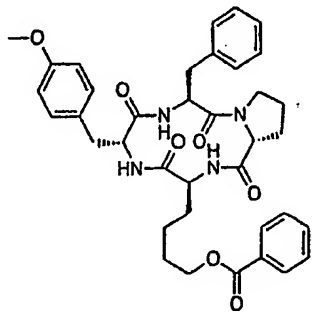
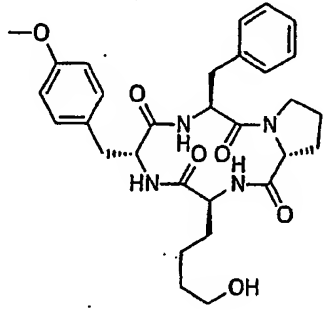
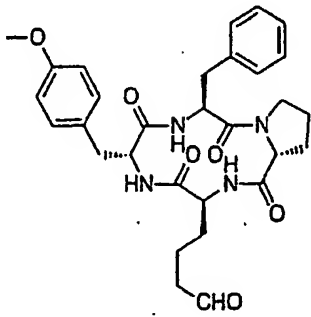
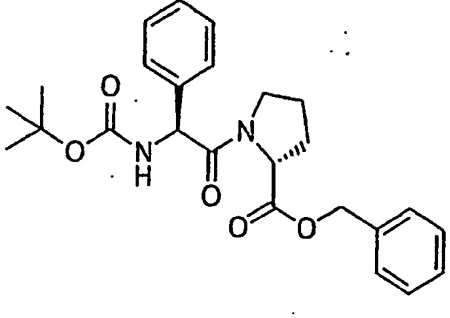
Compound (230)	Compound (231)
	
Compound (232)	Compound (233)
	
Compound (234)	Compound (235)
	
Compound (236)	Compound (237)
	

Table 2-30

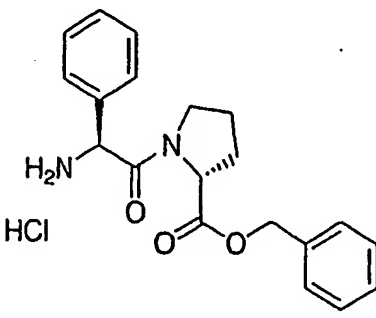
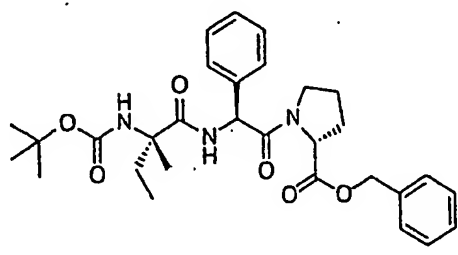
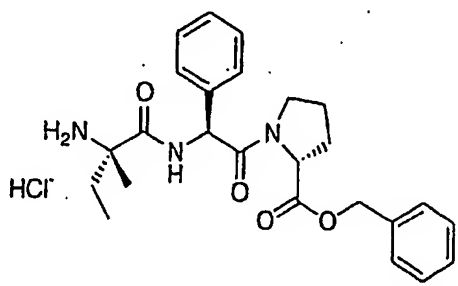
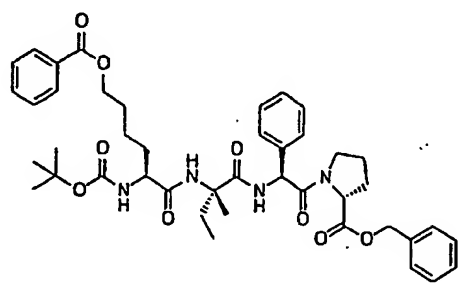
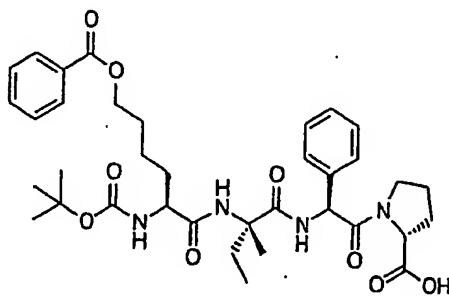
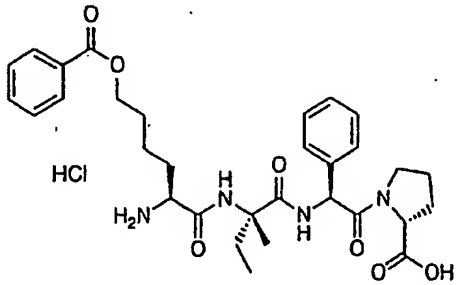
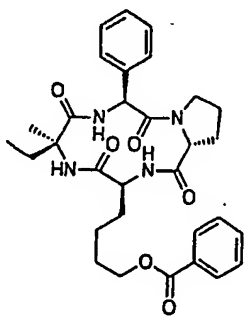
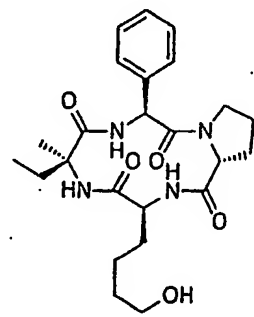
Compound (238)	Compound (239)
	
Compound (240)	Compound (241)
	
Compound (242)	Compound (243)
	
Compound (244)	Compound (245)
	

Table 2-31

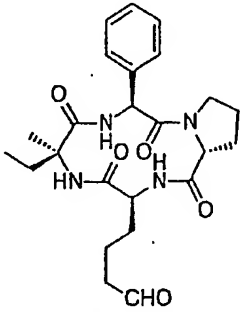
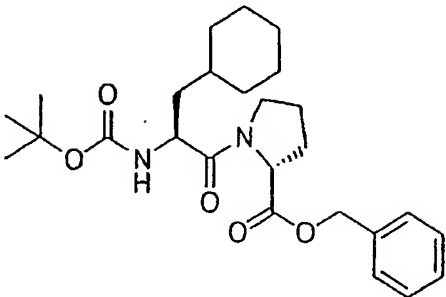
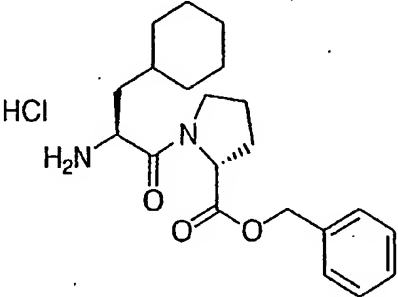
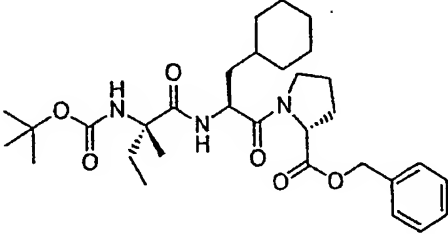
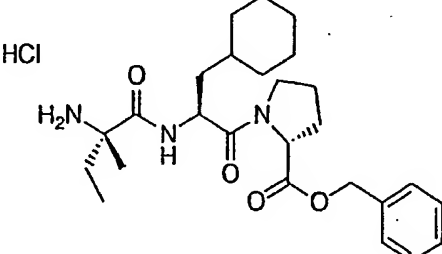
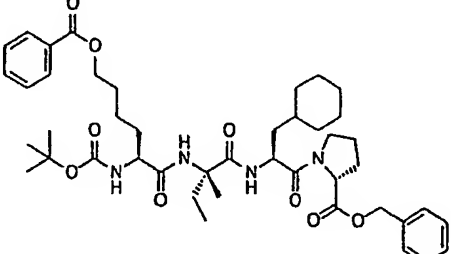
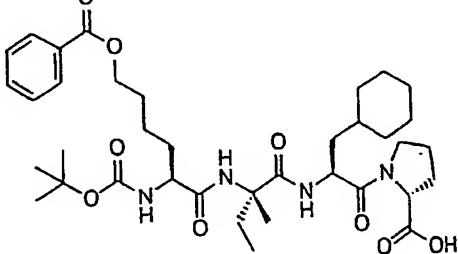
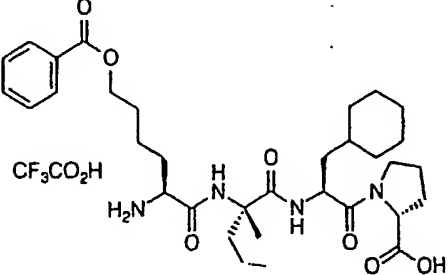
Compound (246)	Compound (247)
	
Compound (248)	Compound (249)
	
Compound (250)	Compound (251)
	
Compound (252)	Compound (253)
	

Table 2-32

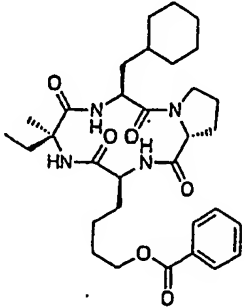
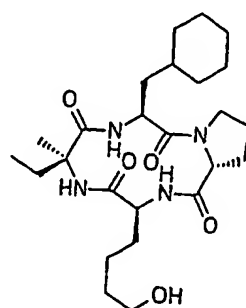
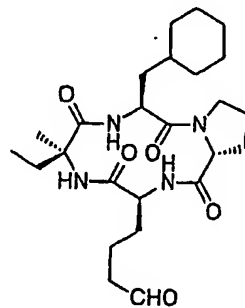
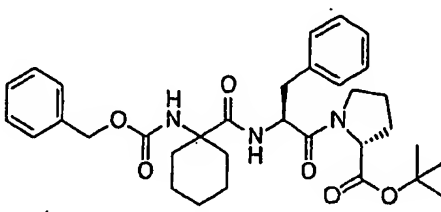
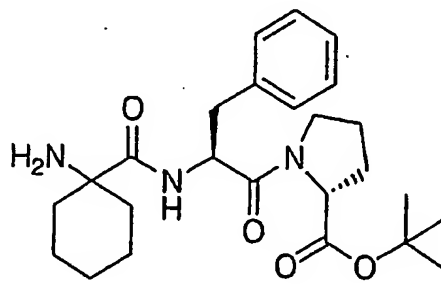
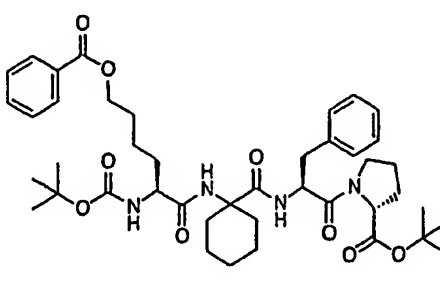
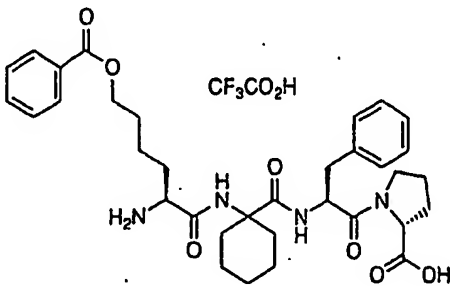
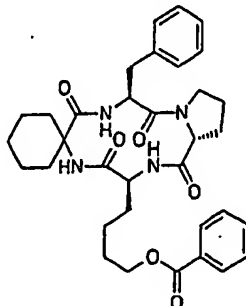
Compound (254)	Compound (255)
	
Compound (256)	Compound (257)
	
Compound (258)	Compound (259)
	
Compound (260)	Compound (261)
	

Table 2-33

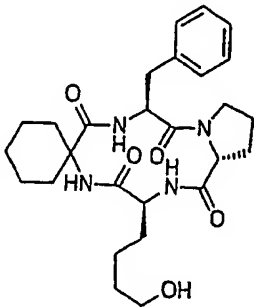
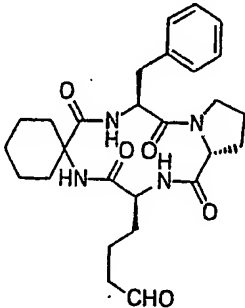
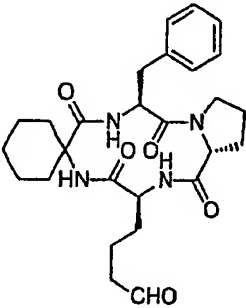
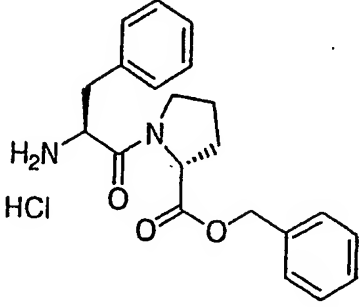
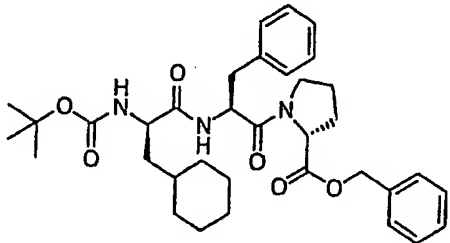
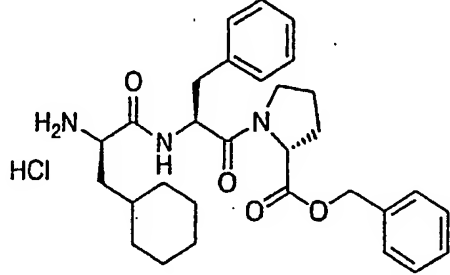
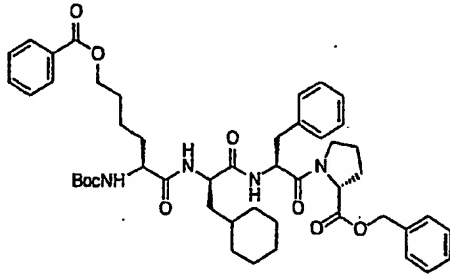
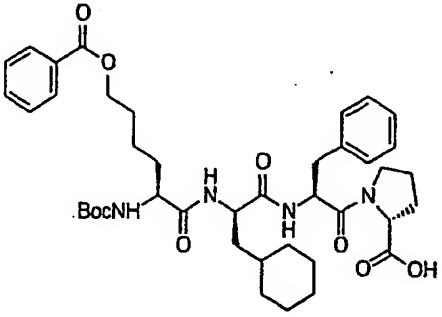
Compound (262)	Compound (263)
	
Compound (264)	Compound (265)
	
Compound (266)	Compound (267)
	
Compound (268)	Compound (269)
	

Table 2-34

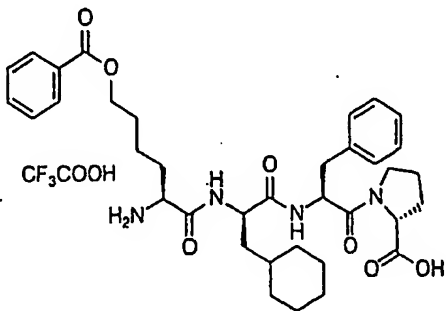
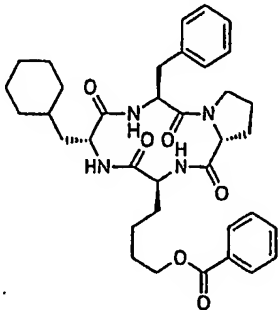
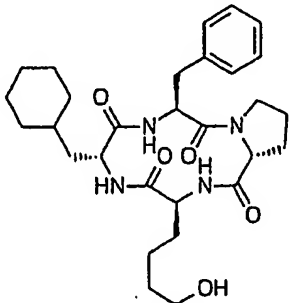
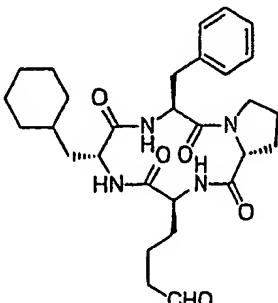
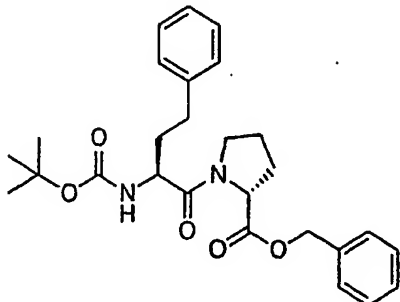
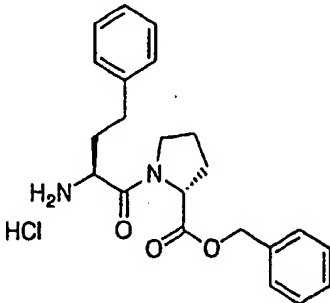
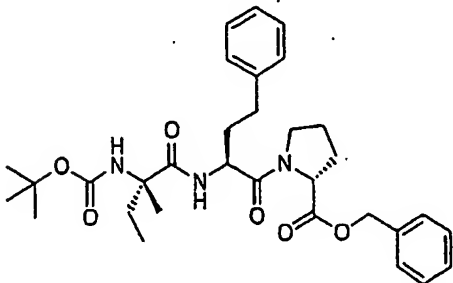
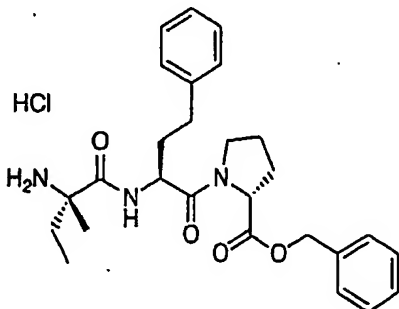
Compound (270)	Compound (271)
	
Compound (272)	Compound (273)
	
Compound (274)	Compound (275)
	
Compound (276)	Compound (277)
	

Table 2-35

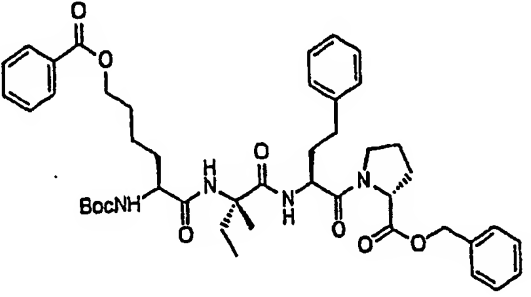
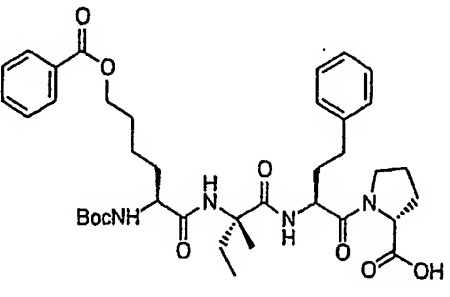
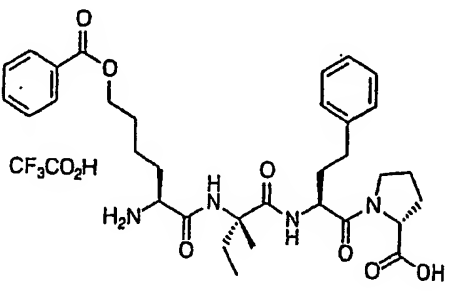
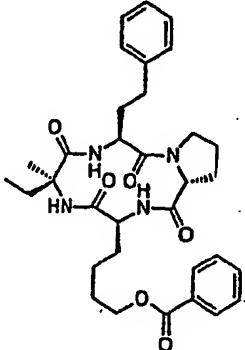
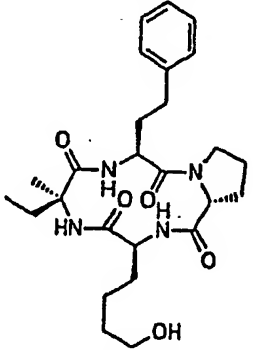
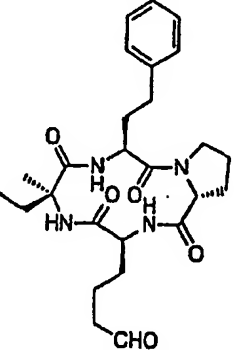
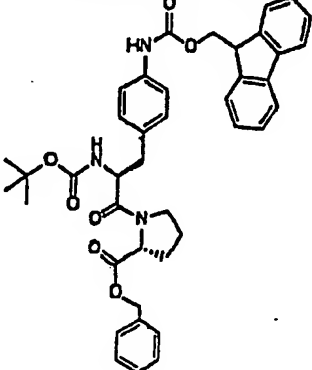
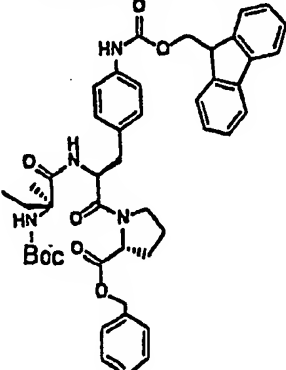
Compound (278)	Compound (279)
	
Compound (280)	Compound (281)
	
Compound (282)	Compound (283)
	
Compound (284)	Compound (285)
	

Table 2-36

Compound (286)	Compound (287)
Compound (288)	Compound (289)
Compound (290)	Compound (291)
Compound (292)	Compound (293)

Table 2-37

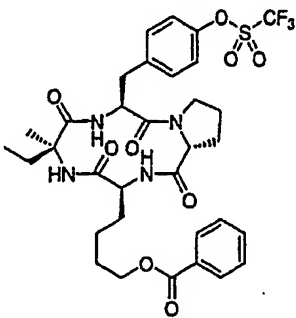
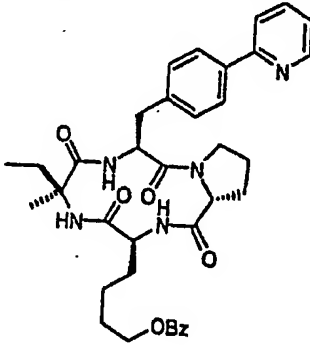
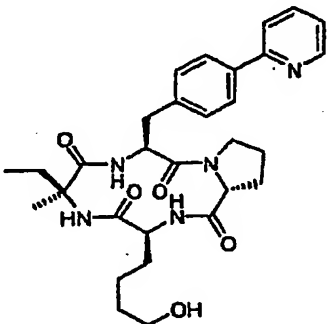
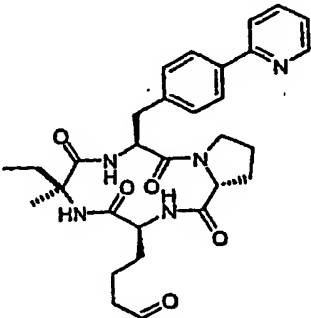
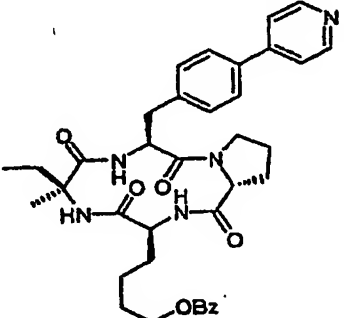
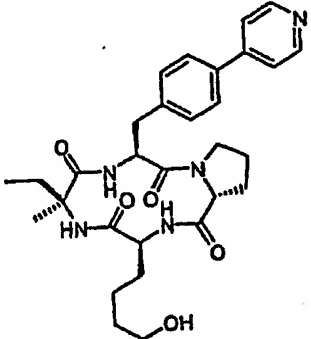
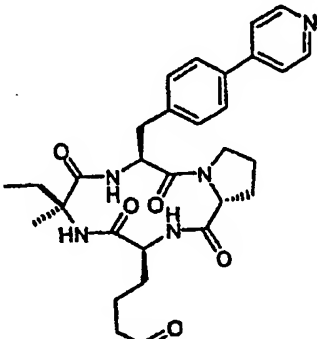
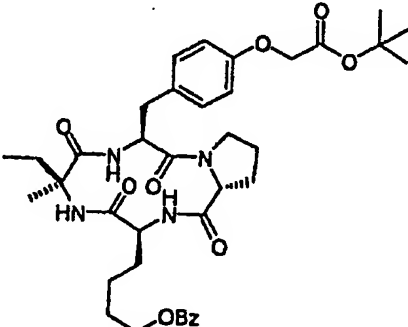
Compound (294)	Compound (295)
	
Compound (296)	Compound (297)
	
Compound (298)	Compound (299)
	
Compound (300)	Compound (301)
	

Table 2-38

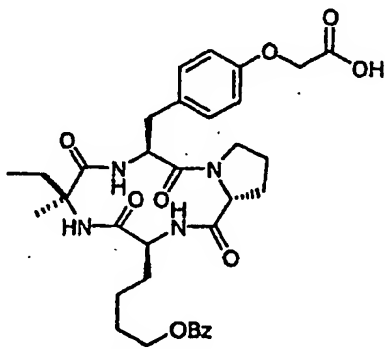
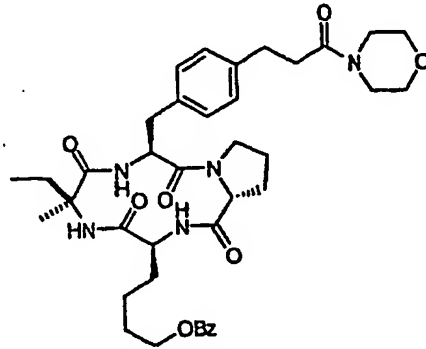
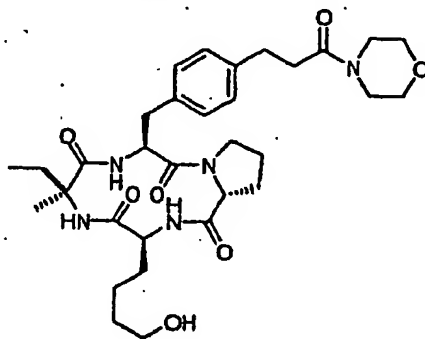
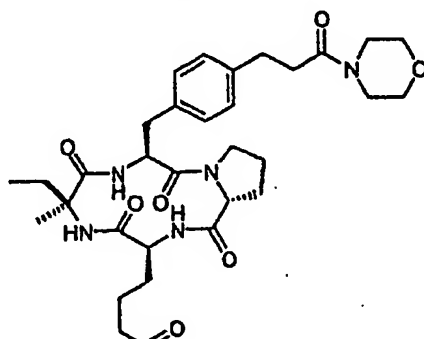
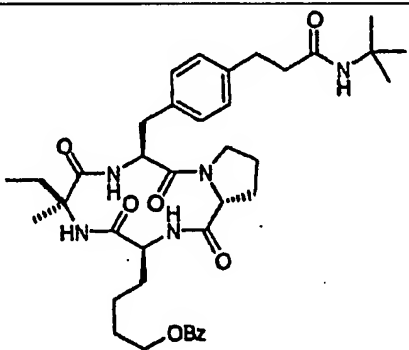
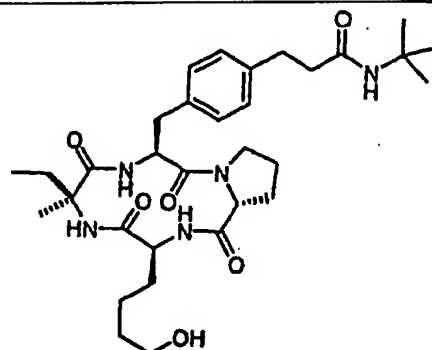
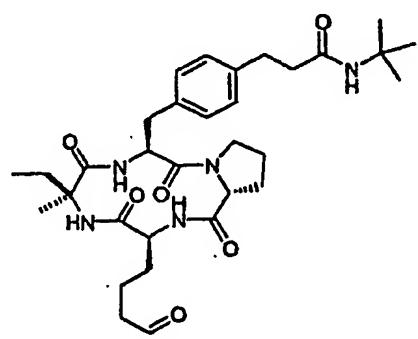
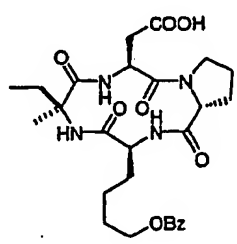
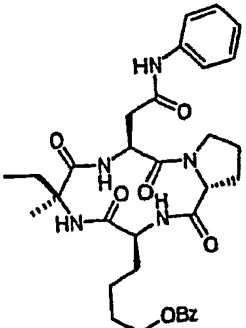
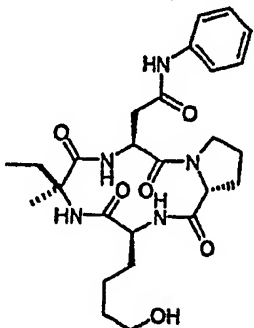
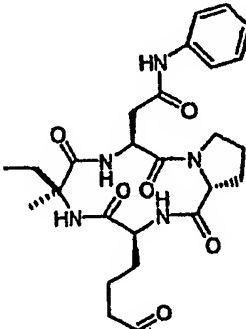
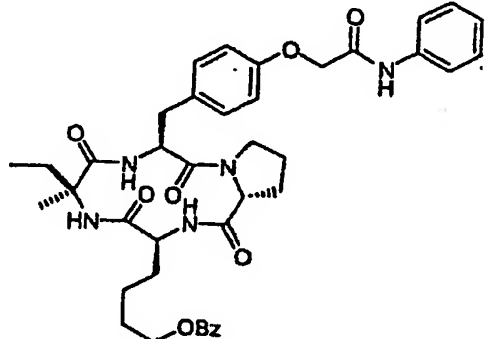
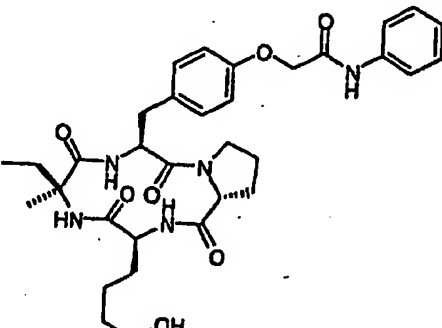
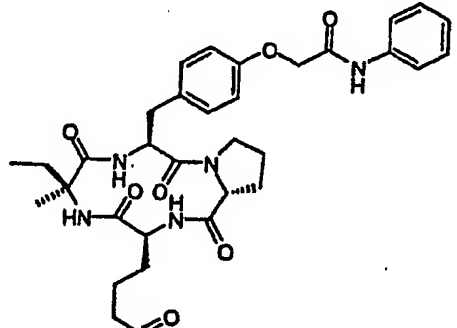
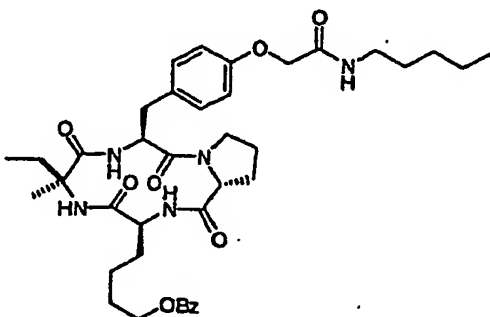
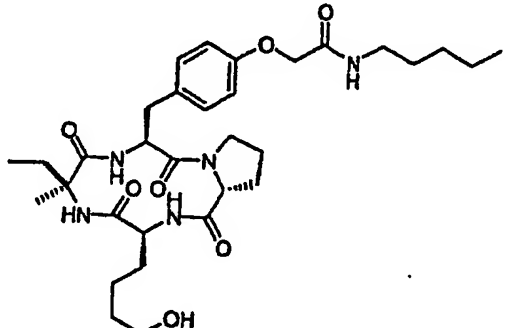
Compound (302)	Compound (303)
	
Compound (304)	Compound (305)
	
Compound (306)	Compound (307)
	
Compound (308)	Compound (309)
	

Table 2-39

Compound (310)	Compound (311)
	
Compound (312)	Compound (313)
	
Compound (314)	Compound (315)
	
Compound (316)	Compound (317)
	

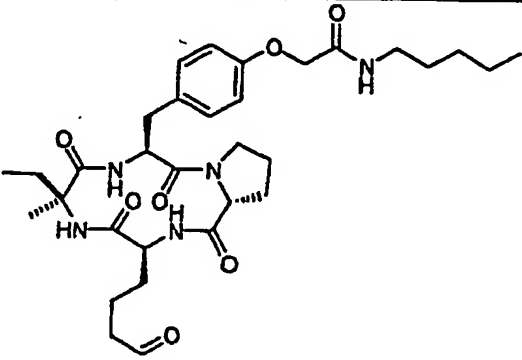
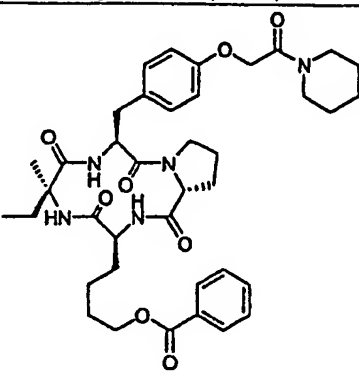
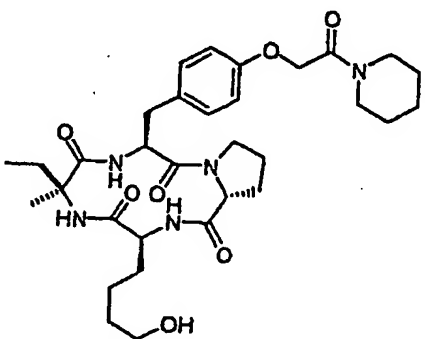
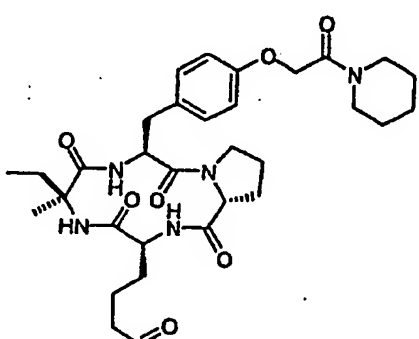
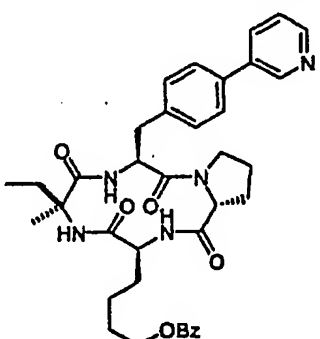
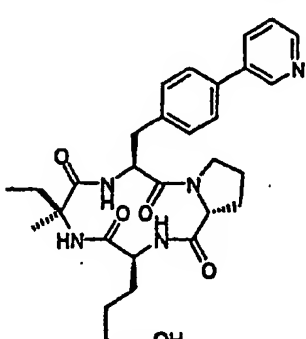
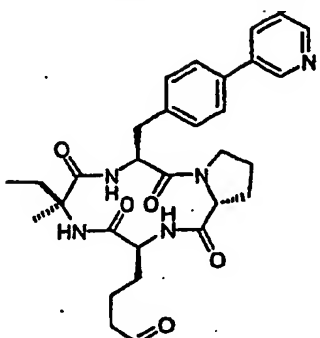
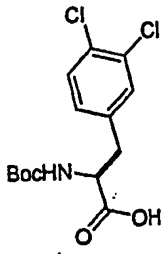
Compound (318)	Compound (319)
	
Compound (320)	Compound (321)
	
Compound (322)	Compound (323)
	
Compound (324)	Compound (325)
	

Table 2-41

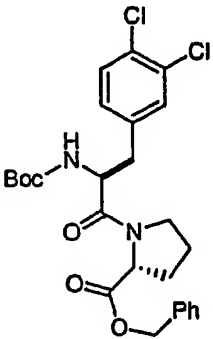
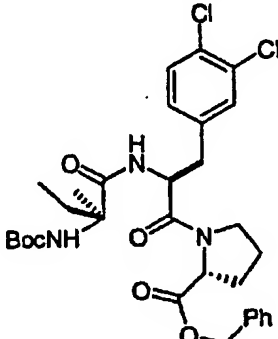
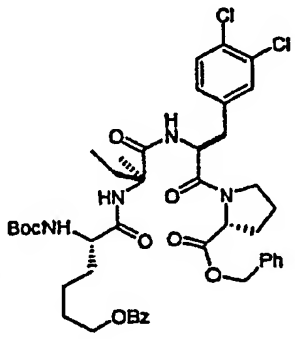
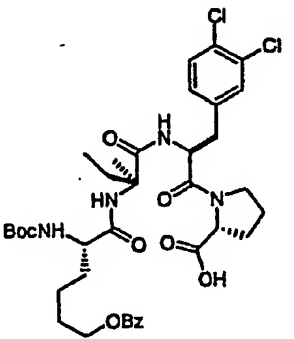
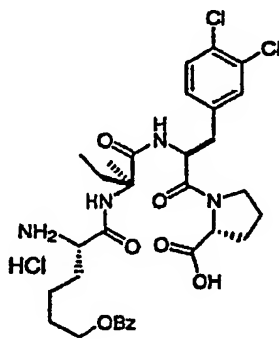
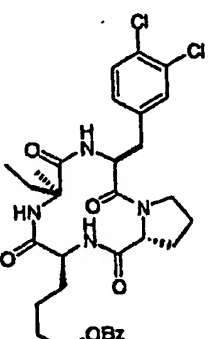
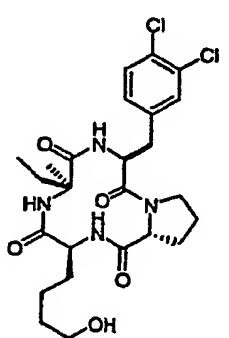
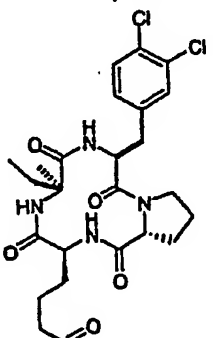
Compound (326)	Compound (327)
	
Compound (328)	Compound (329)
	
Compound (330)	Compound (331)
	
Compound (332)	Compound (333)
	

Table 2-42

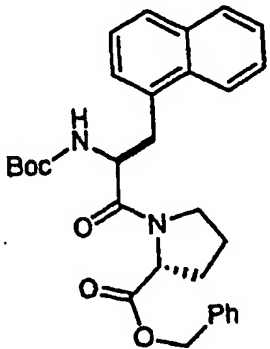
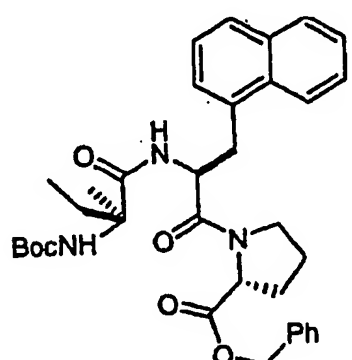
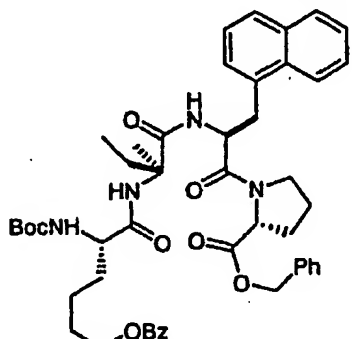
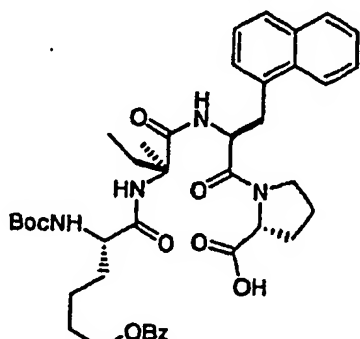
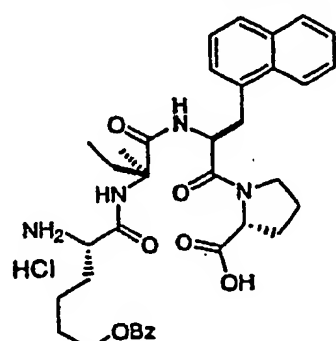
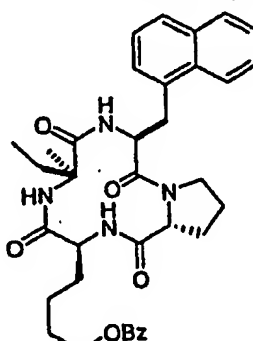
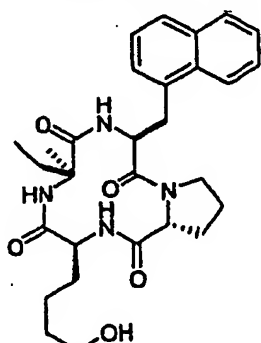
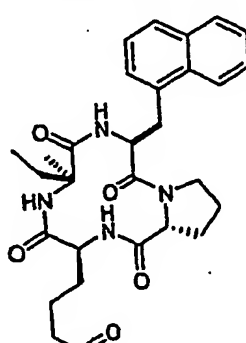
Compound (334)	Compound (335)
	
Compound (336)	Compound (337)
	
Compound (338)	Compound (339)
	
Compound (340)	Compound (341)
	

Table 2-43

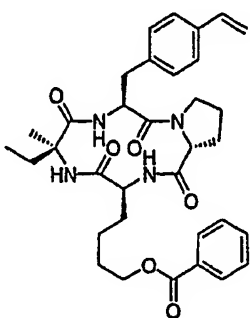
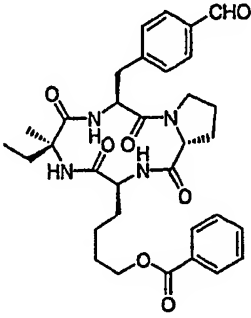
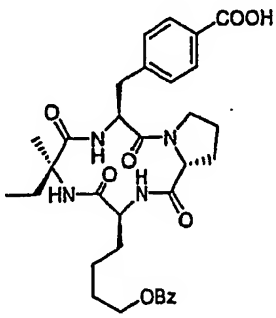
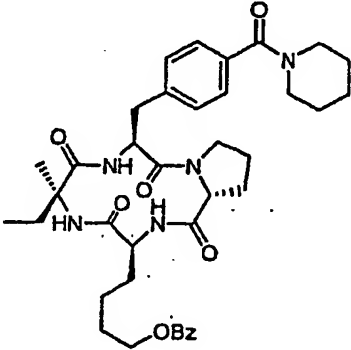
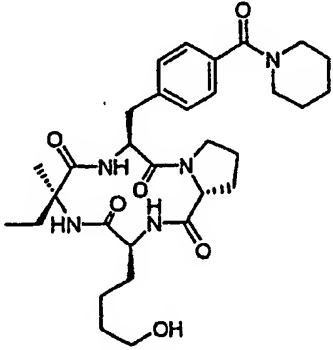
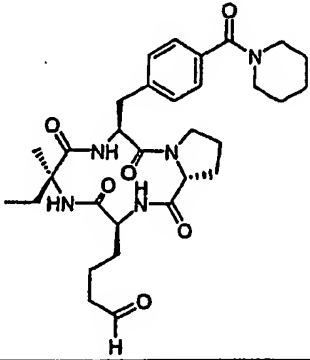
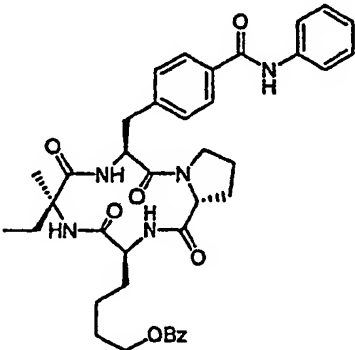
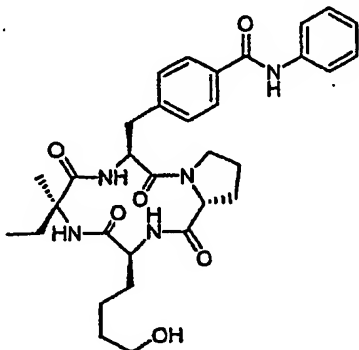
Compound (342)	Compound (343)
	
Compound (344)	Compound (345)
	
Compound (346)	Compound (347)
	
Compound (348)	Compound (349)
	

Table 2-44

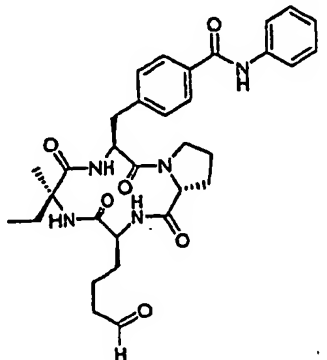
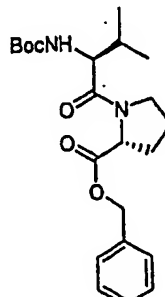
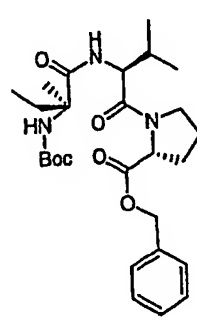
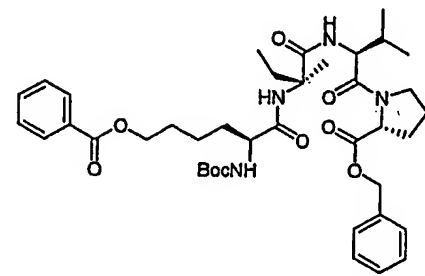
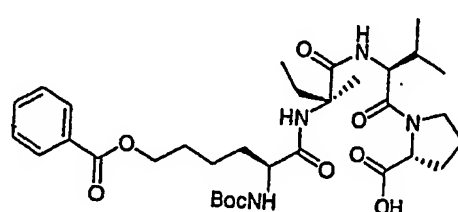
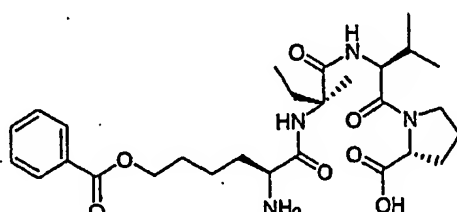
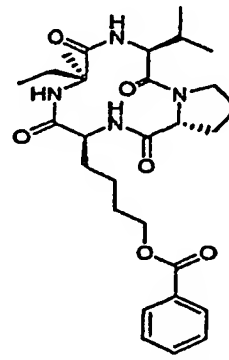
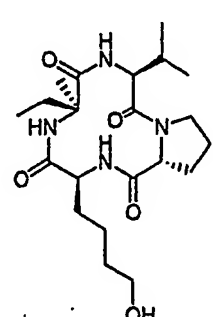
Compound (350)	Compound (351)
	
Compound (352)	Compound (353)
	
Compound (354)	Compound (355)
	
Compound (356)	Compound (357)
	

Table 2-45

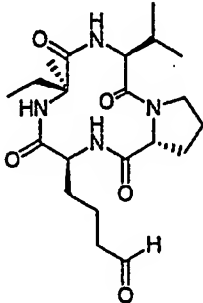
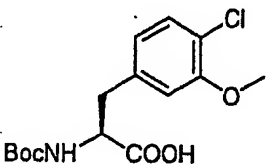
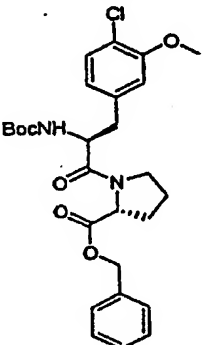
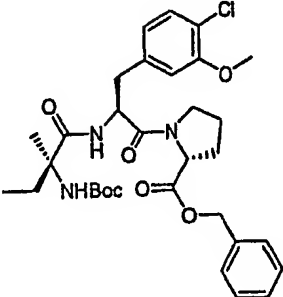
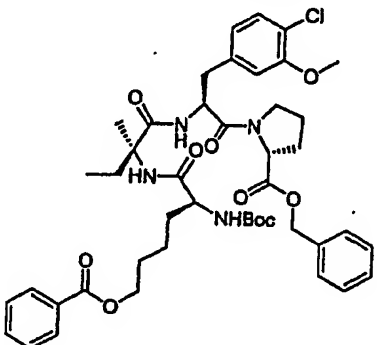
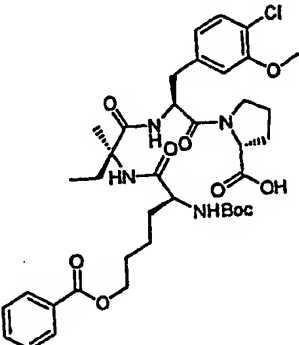
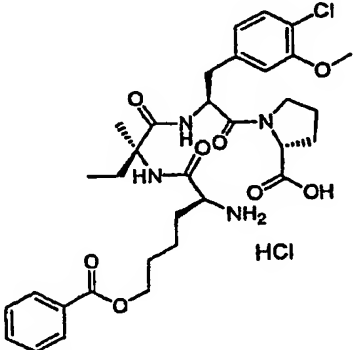
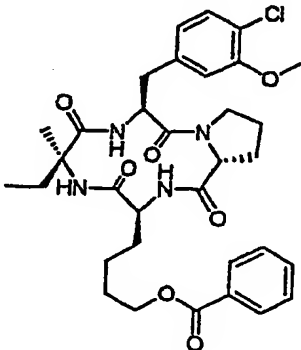
Compound (358)	Compound (359)
	
Compound (360)	Compound (361)
	
Compound (362)	Compound (363)
	
Compound (364)	Compound (365)
	

Table 2-46

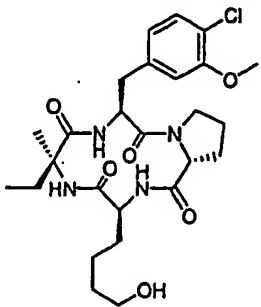
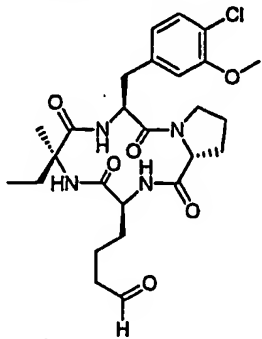
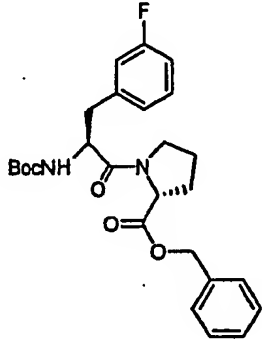
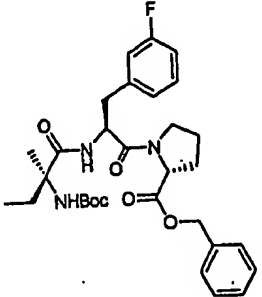
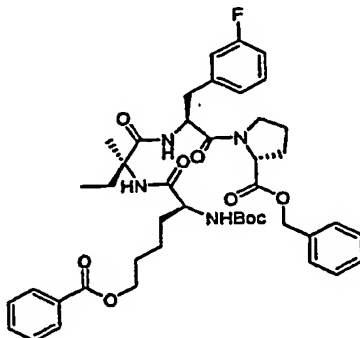
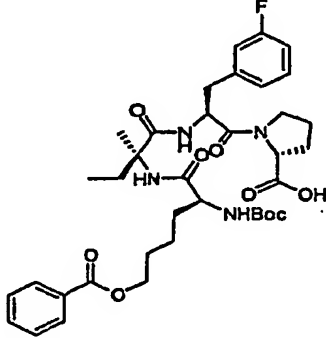
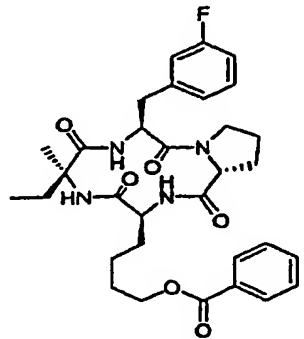
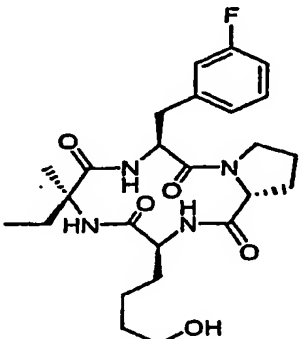
Compound (366)	Compound (367)
	
Compound (368)	Compound (369)
	
Compound (370)	Compound (371)
	
Compound (372)	Compound (373)
	

Table 2-47

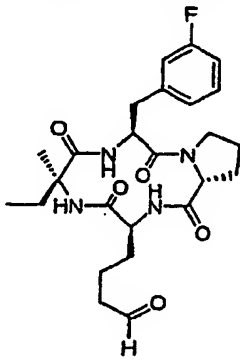
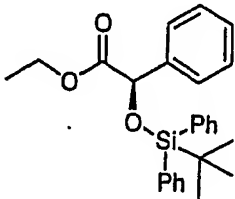
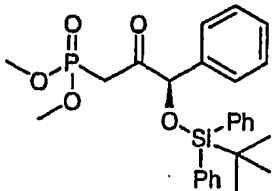
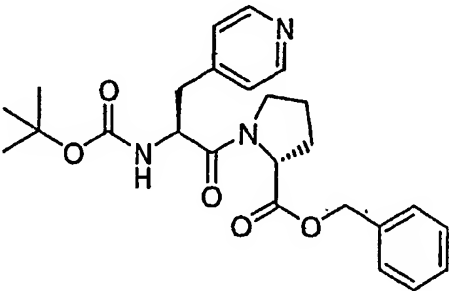
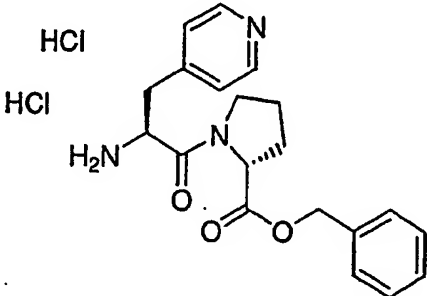
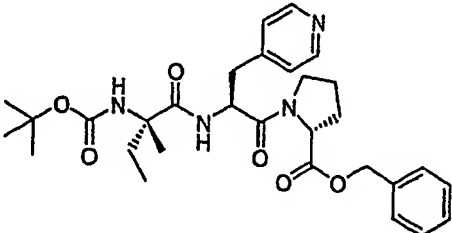
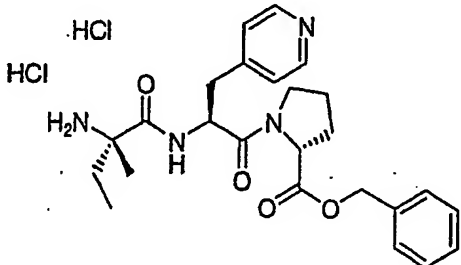
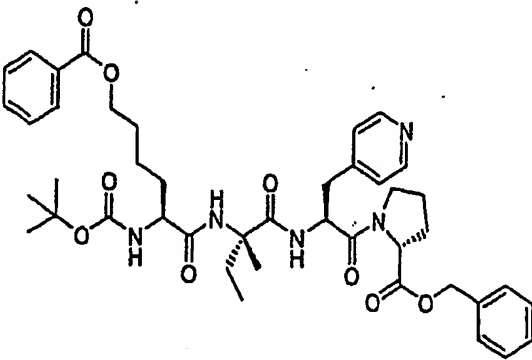
Compound (374)	Compound (375)
	
Compound (376)	Compound (377)
	
Compound (378)	Compound (379)
	
Compound (380)	Compound (381)
	

Table 2-48

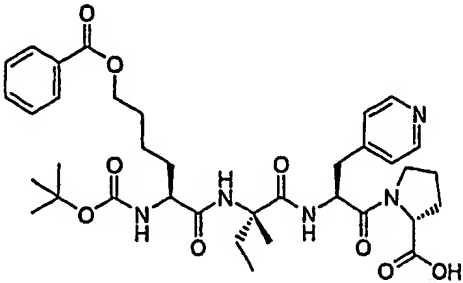
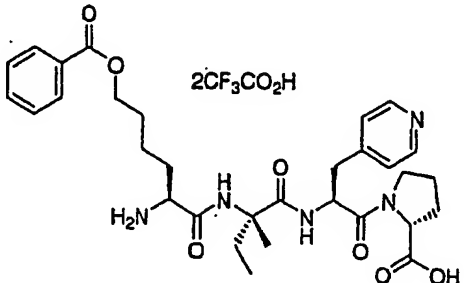
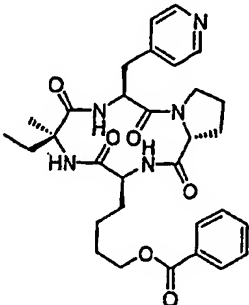
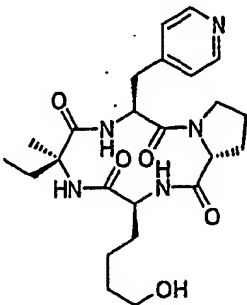
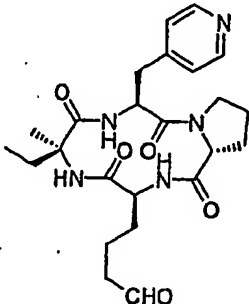
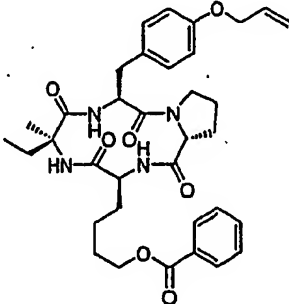
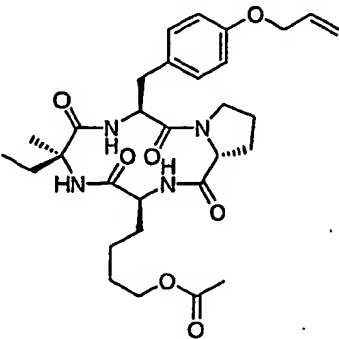
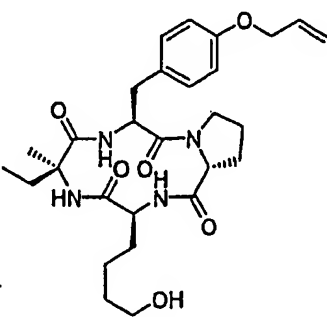
Compound (382)	Compound (383)
	
Compound (384)	Compound (385)
	
Compound (386)	Compound (387)
	
Compound (388)	Compound (389)
	

Table 2-49

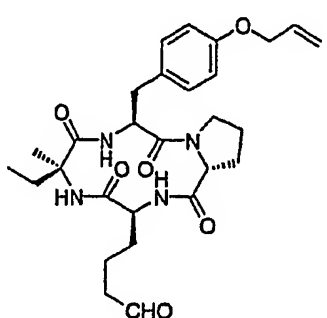
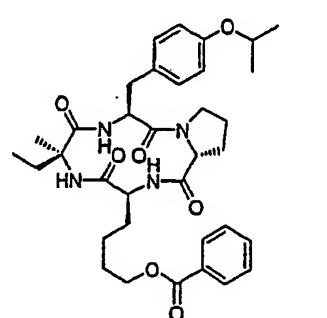
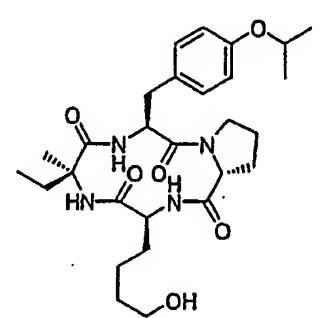
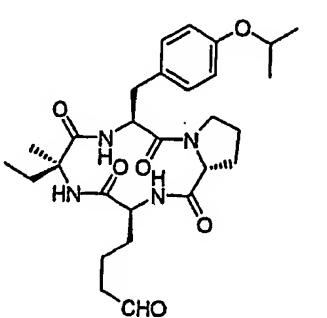
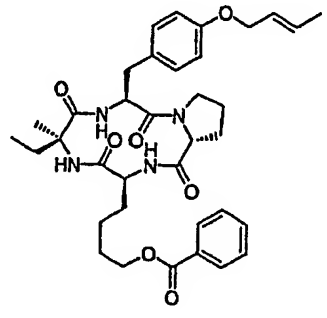
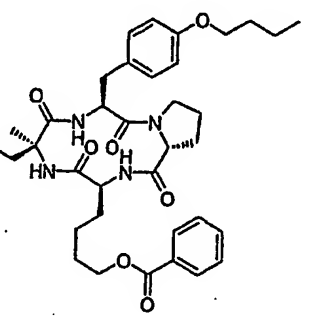
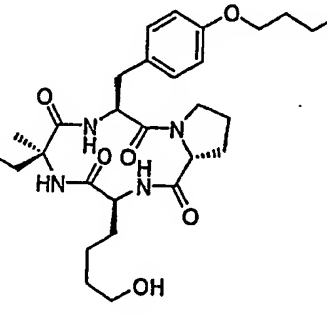
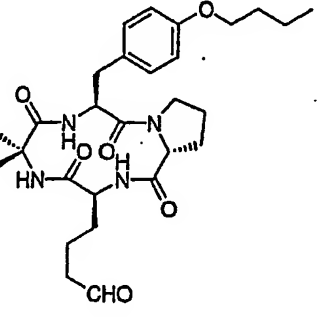
Compound (390)	Compound (391)
	
Compound (392)	Compound (393)
	
Compound (394)	Compound (395)
	
Compound (396)	Compound (397)
	

Table 2-50

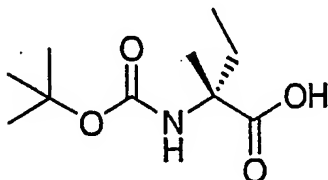
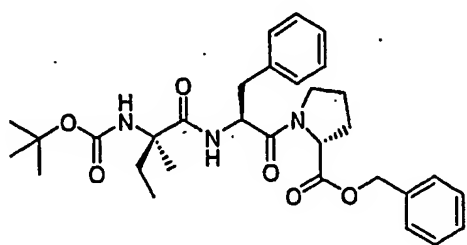
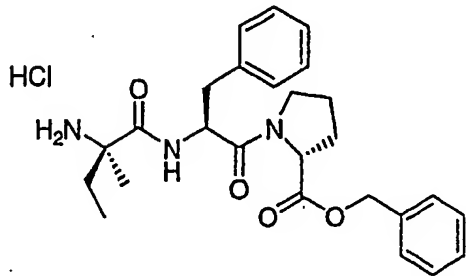
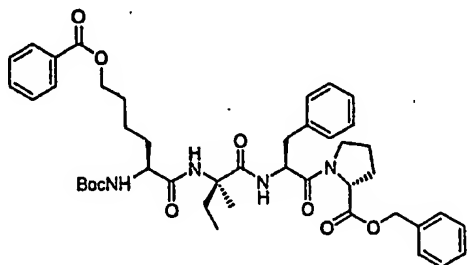
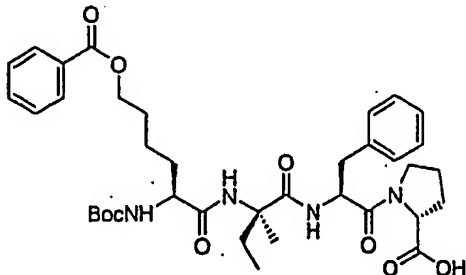
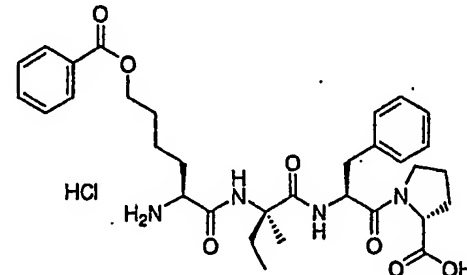
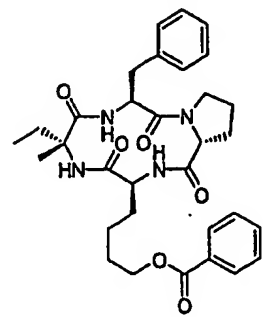
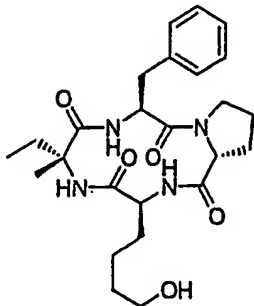
Compound (398)	Compound (399)
	
Compound (400)	Compound (401)
	
Compound (402)	Compound (403)
	
Compound (404)	Compound (405)
	

Table 2-51

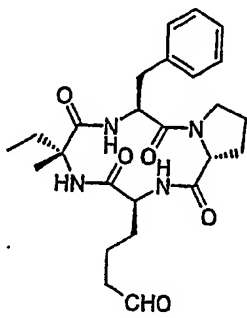
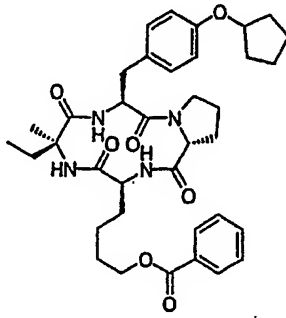
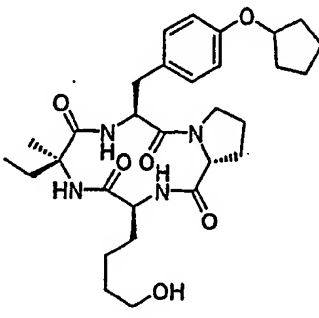
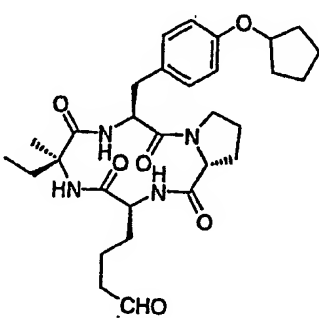
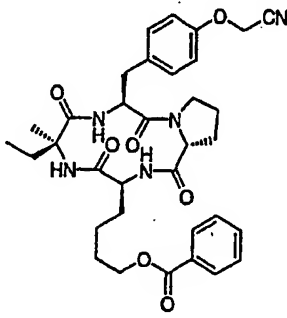
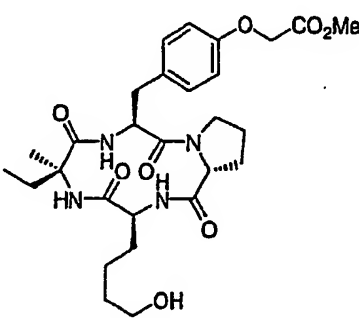
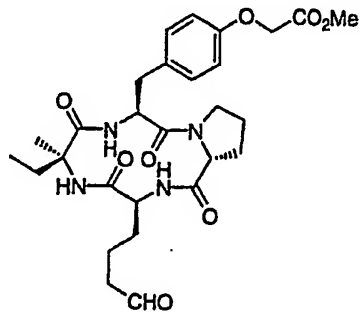
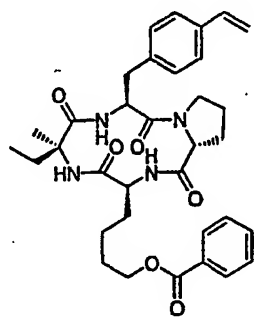
Compound (406)	Compound (407)
	
Compound (408)	Compound (409)
	
Compound (410)	Compound (411)
	
Compound (412)	Compound (413)
	

Table 2-52

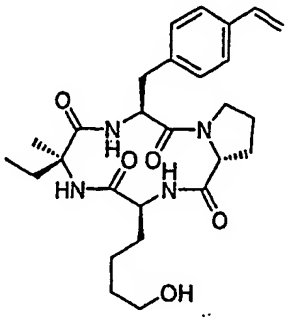
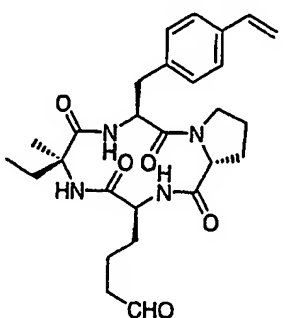
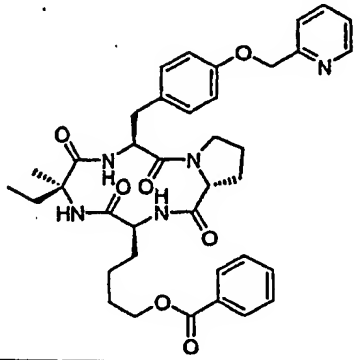
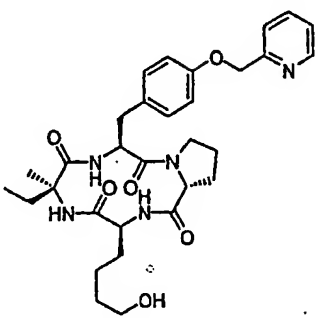
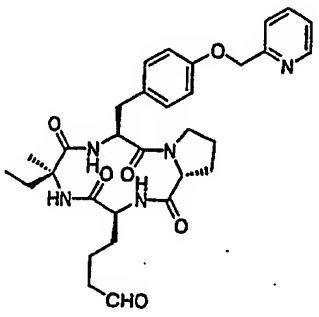
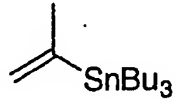
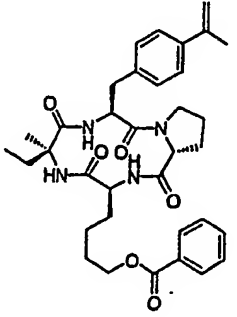
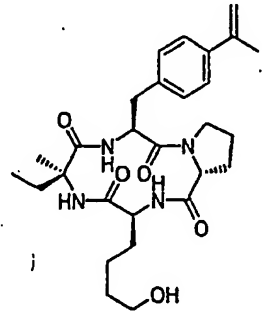
Compound (414)	Compound (415)
	
Compound (416)	Compound (417)
	
Compound (418)	Compound (419)
	
Compound (420)	Compound (421)
	

Table 2-53

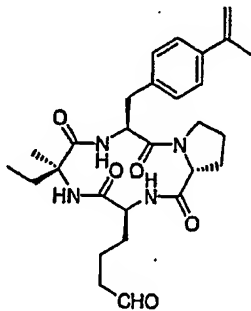
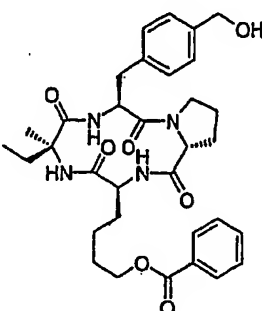
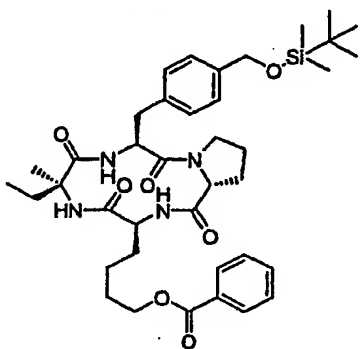
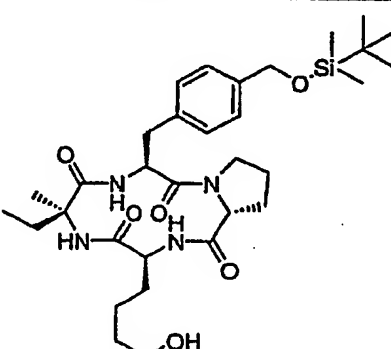
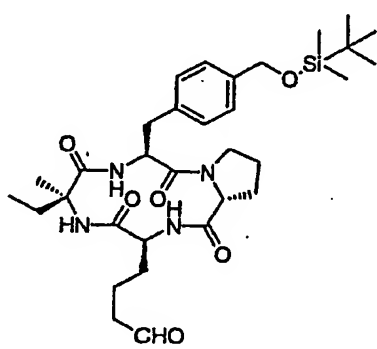
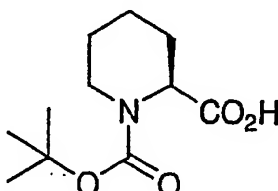
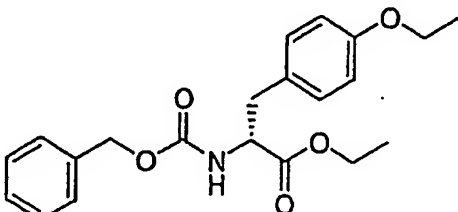
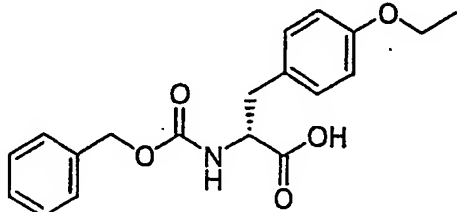
Compound (422)	Compound (423)
	
Compound (424)	Compound (425)
	
Compound (426)	Compound (427)
	
Compound (428)	Compound (429)
	

Table 2-54

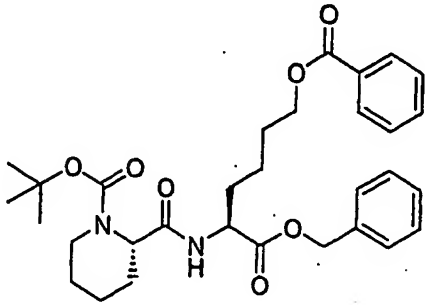
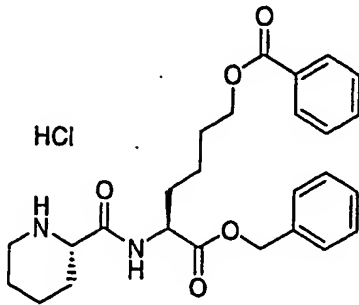
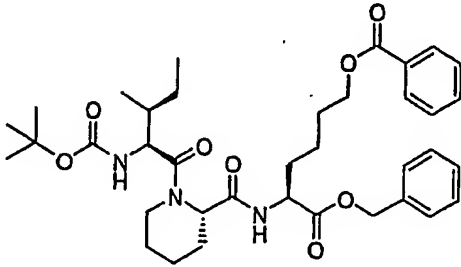
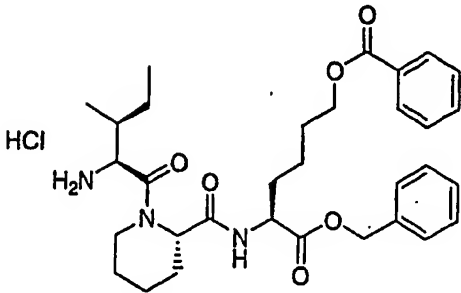
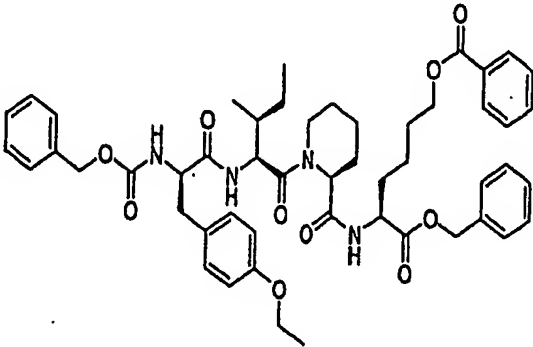
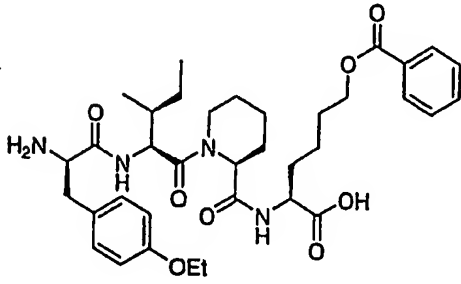
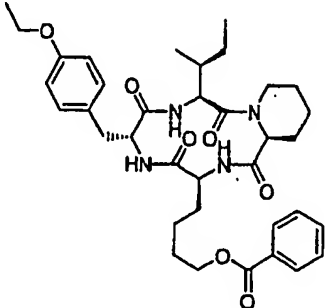
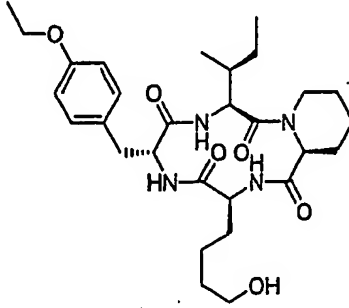
Compound (430)	Compound (431)
	
Compound (432)	Compound (433)
	
Compound (434)	Compound (435)
	
Compound (436)	Compound (437)
	

Table 2-55

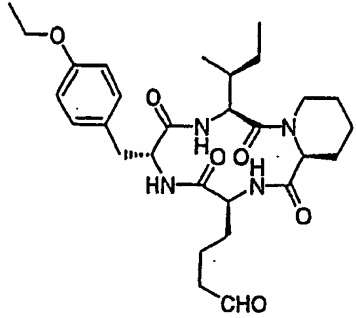
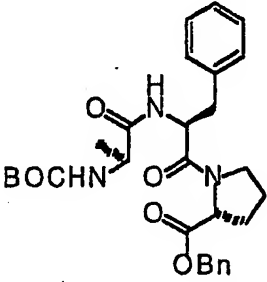
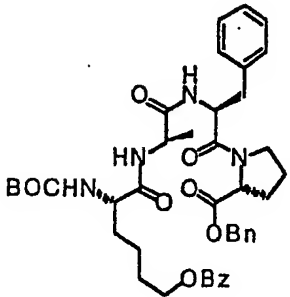
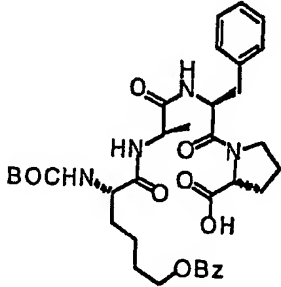
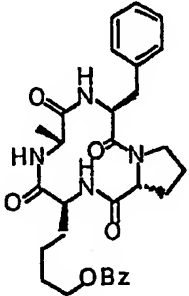
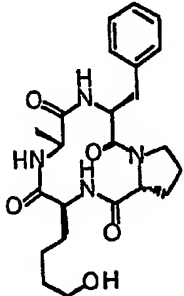
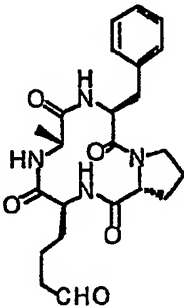
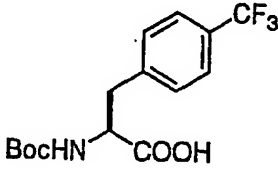
Compound (438)	Compound (439)
	
Compound (440)	Compound (441)
	
Compound (442)	Compound (443)
	
Compound (444)	Compound (445)
	

Table 2-56

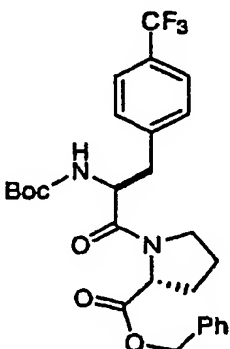
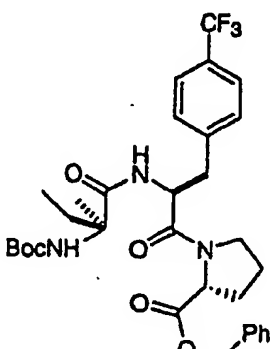
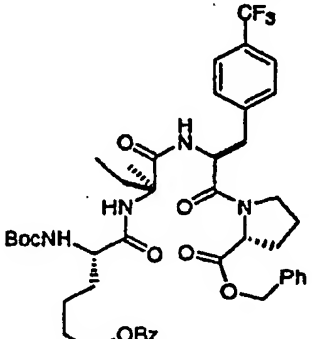
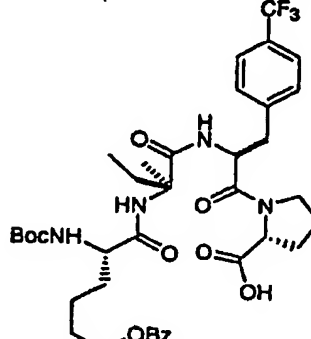
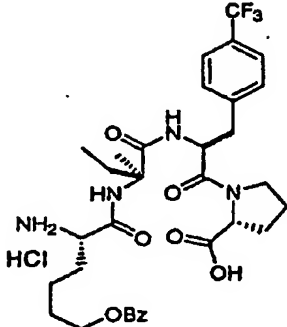
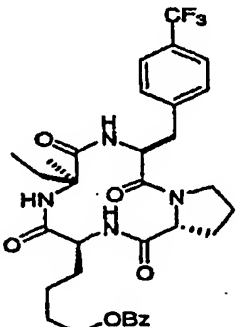
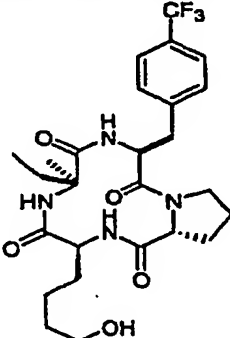
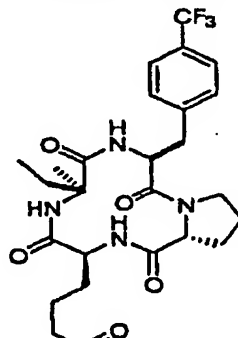
Compound (446)	Compound (447)
	
Compound (448)	Compound (449)
	
Compound (450)	Compound (451)
	
Compound (452)	Compound (453)
	

Table 2-57

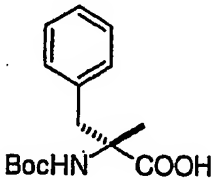
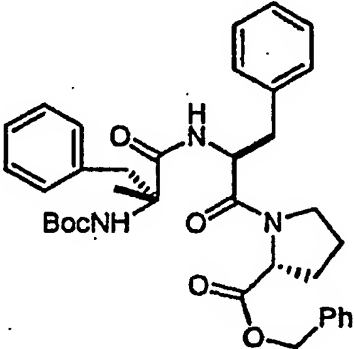
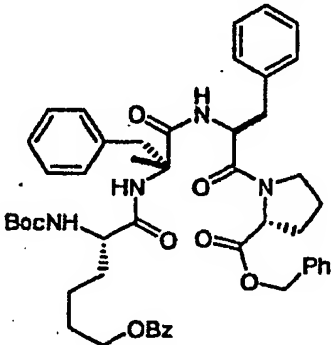
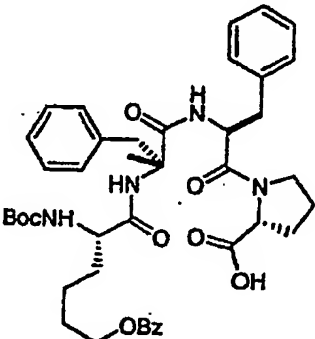
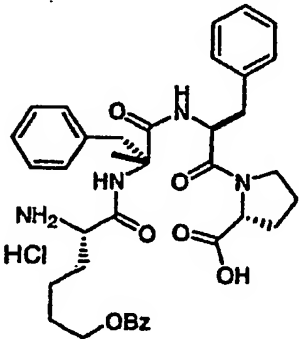
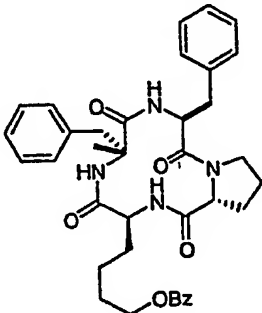
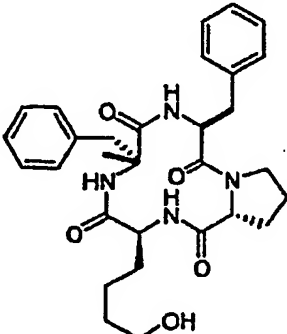
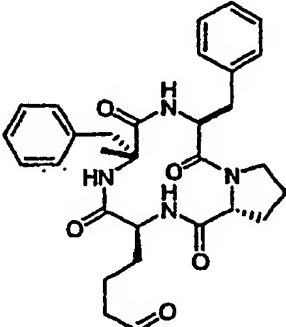
Compound (454)	Compound (455)
	
Compound (456)	Compound (457)
	
Compound (458)	Compound (459)
	
Compound (460)	Compound (461)
	

Table 2-58

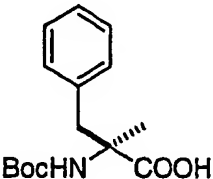
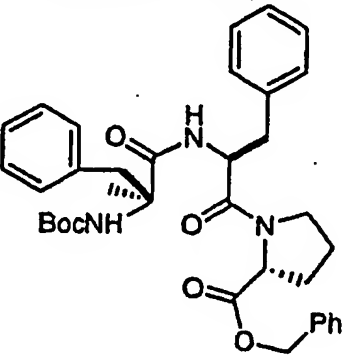
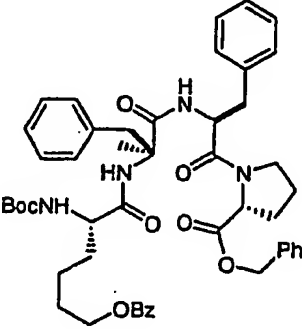
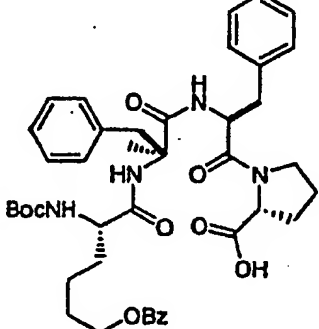
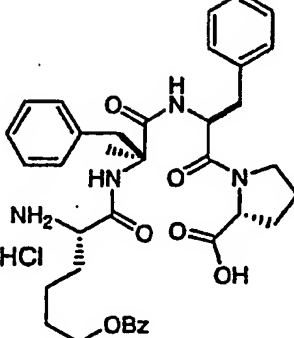
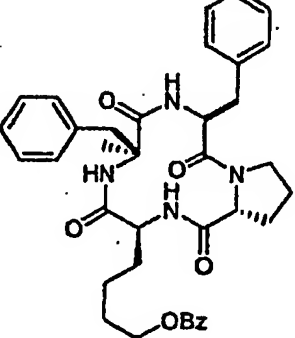
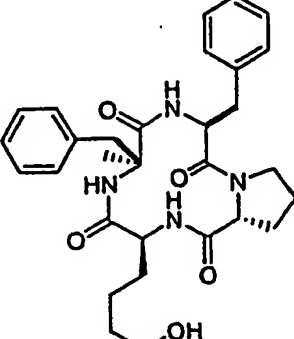
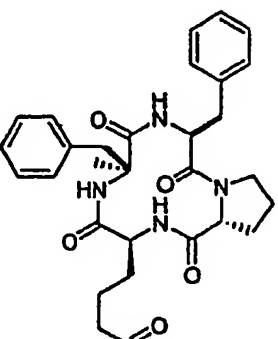
Compound (462)	Compound (463)
	
Compound (464)	Compound (465)
	
Compound (466)	Compound (467)
	
Compound (468)	Compound (469)
	

Table 2-59

Compound (470)	Compound (471)
Compound (472)	Compound (473)
Compound (474)	Compound (475)
Compound (476)	Compound (477)

Table 2-60

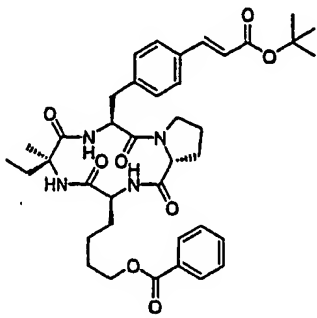
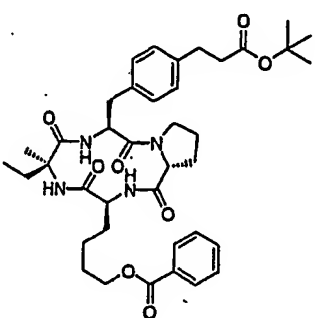
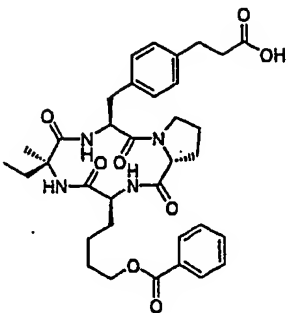
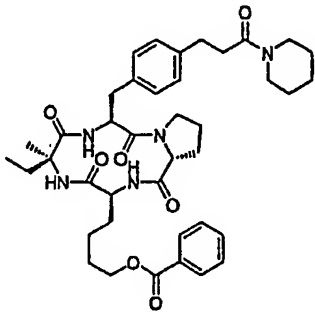
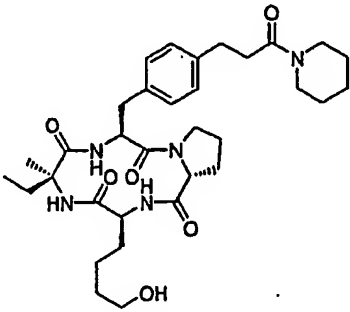
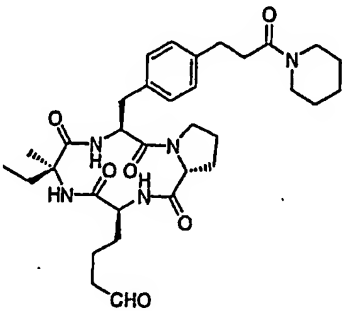
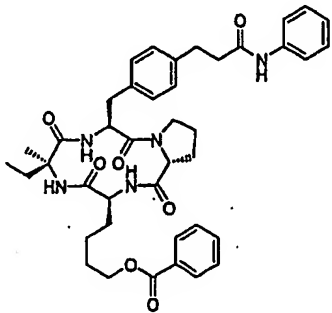
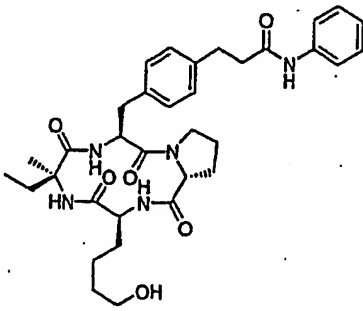
Compound (478)	Compound (479)
	
Compound (480)	Compound (481)
	
Compound (482)	Compound (483)
	
Compound (484)	Compound (485)
	

Table 2-61

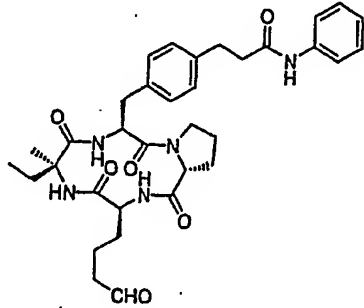
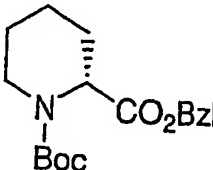
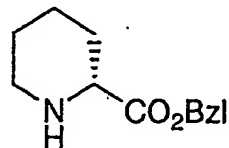
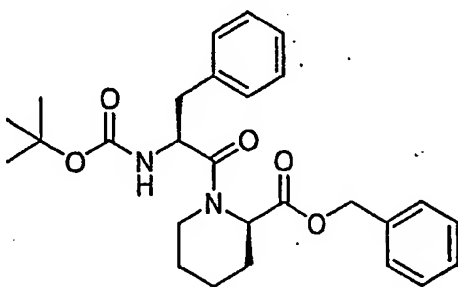
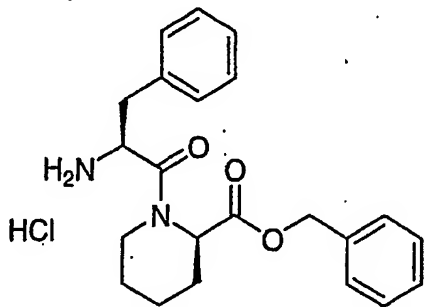
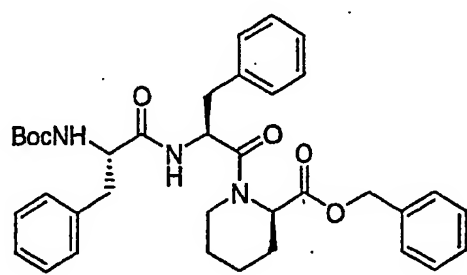
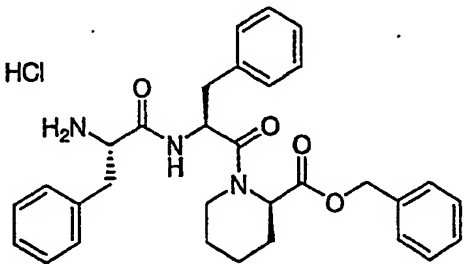
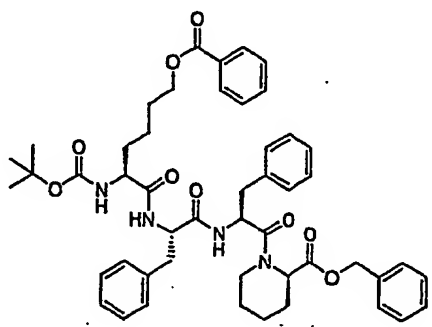
Compound (486)	Compound (487)
	
Compound (488)	Compound (489)
 HCl	
Compound (490)	Compound (491)
 HCl	
Compound (492)	Compound (493)
 HCl	

Table 2-62

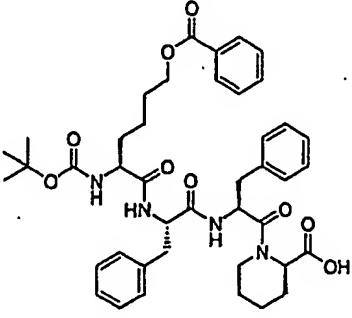
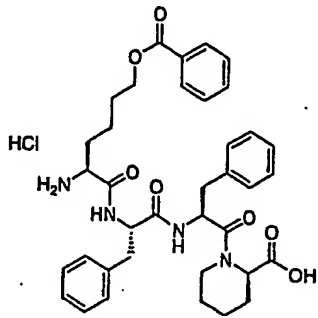
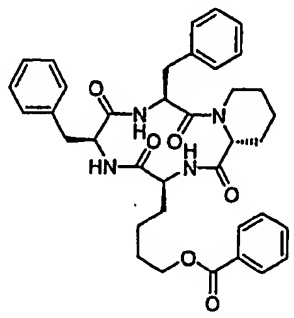
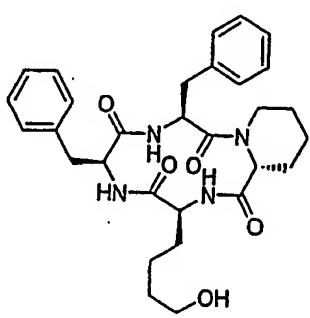
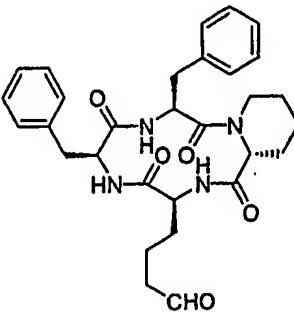
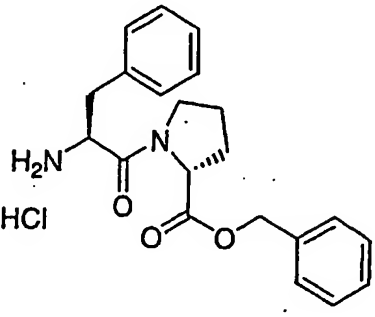
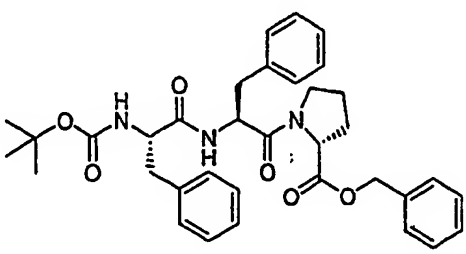
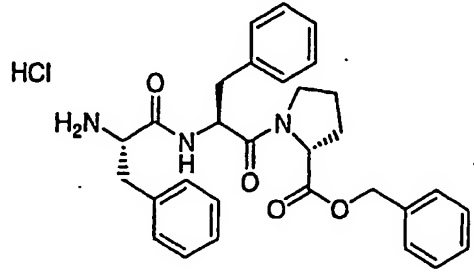
Compound (494)	Compound (495)
	
Compound (496)	Compound (497)
	
Compound (498)	Compound (499)
	
Compound (500)	Compound (501)
	

Table 2-63

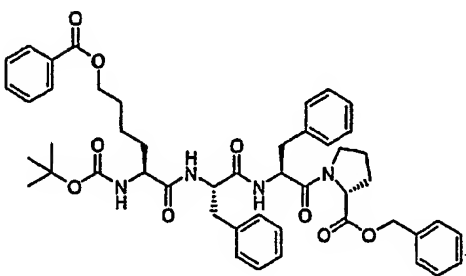
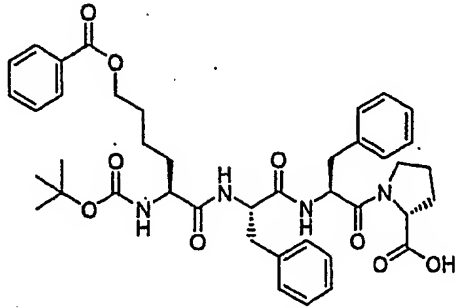
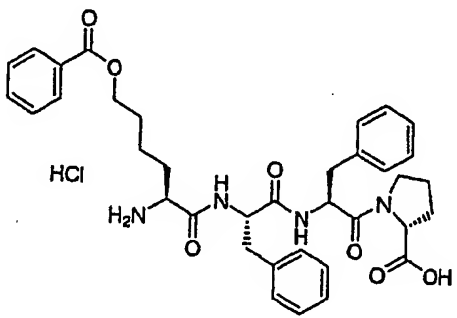
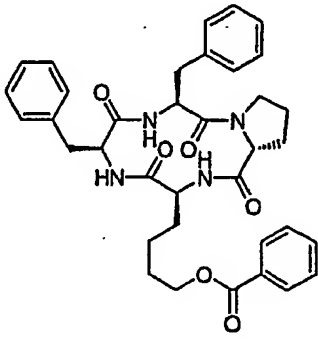
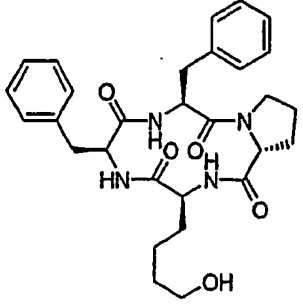
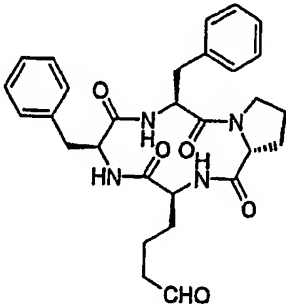
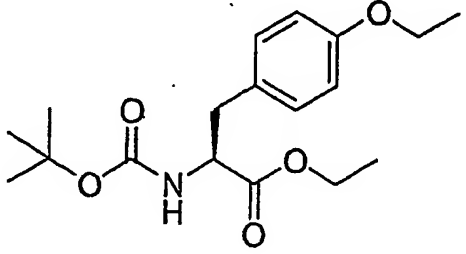
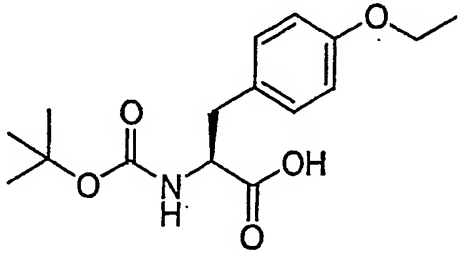
Compound (502)	Compound (503)
	
Compound (504)	Compound (505)
	
Compound (506)	Compound (507)
	
Compound (508)	Compound (509)
	

Table 2-64

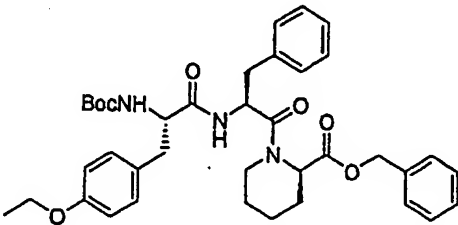
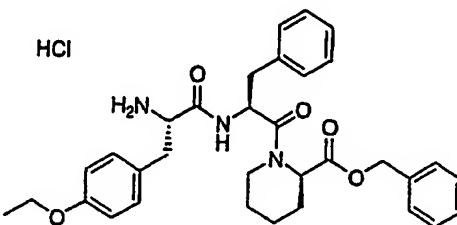
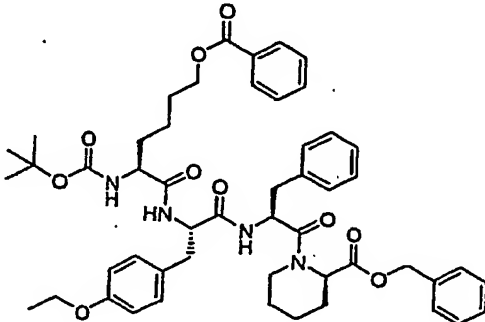
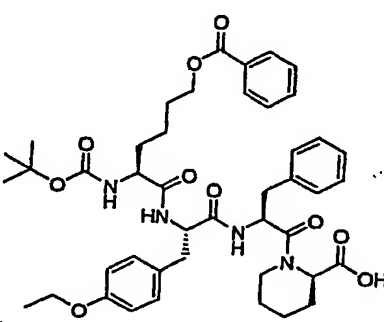
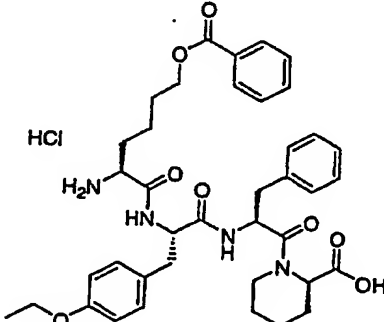
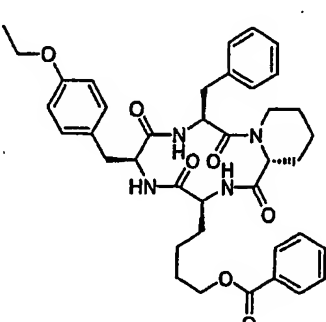
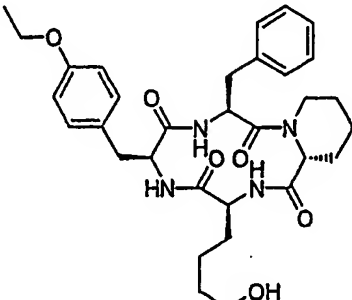
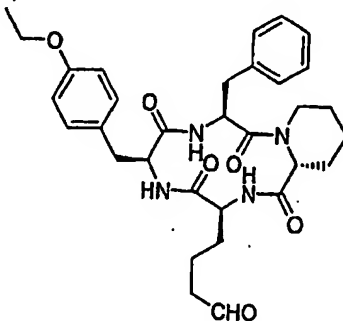
Compound (510)	Compound (511)
	
Compound (512)	Compound (513)
	
Compound (514)	Compound (515)
	
Compound (516)	Compound (517)
	

Table 2-65

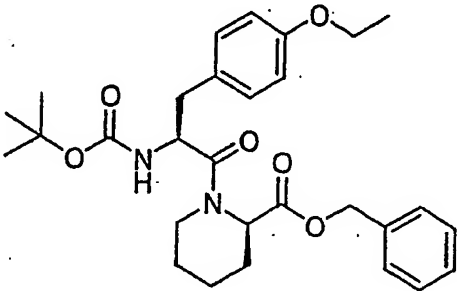
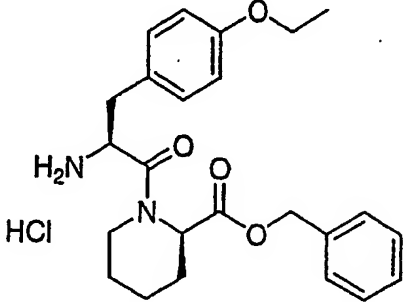
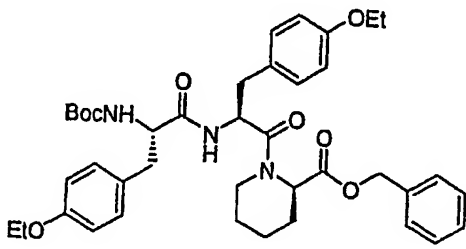
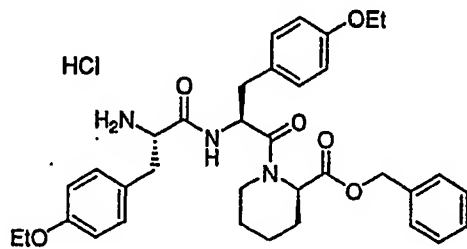
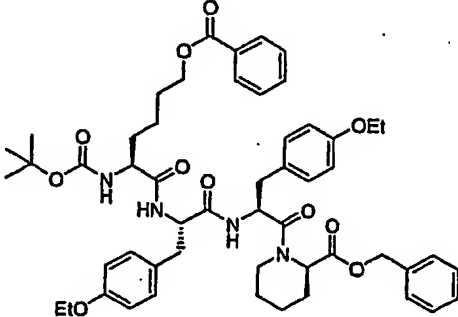
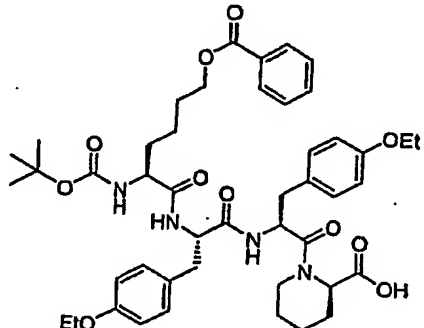
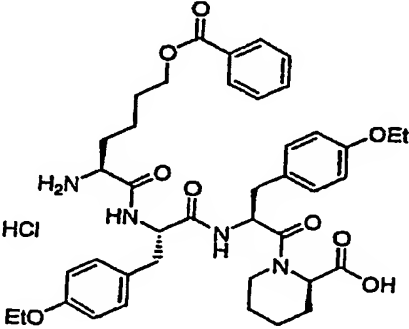
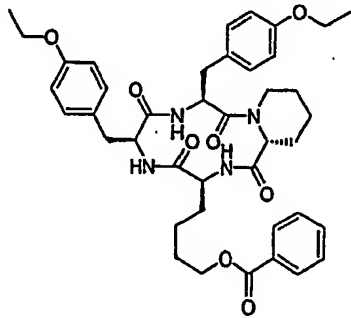
Compound (518)	Compound (519)
	
Compound (520)	Compound (521)
	
Compound (522)	Compound (523)
	
Compound (524)	Compound (525)
	

Table 2-66

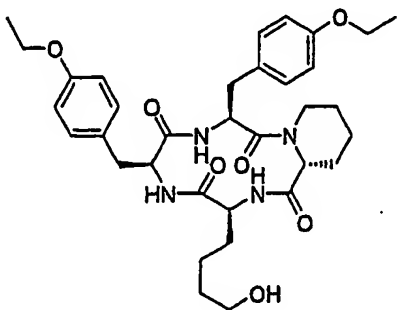
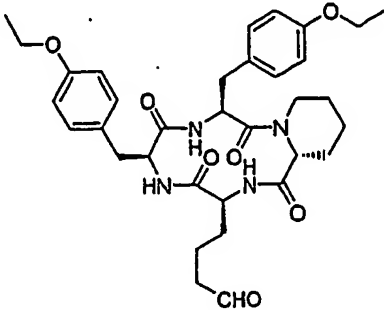
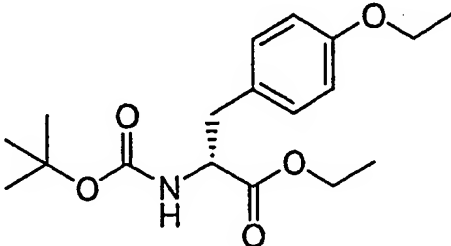
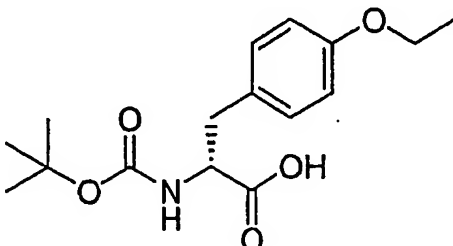
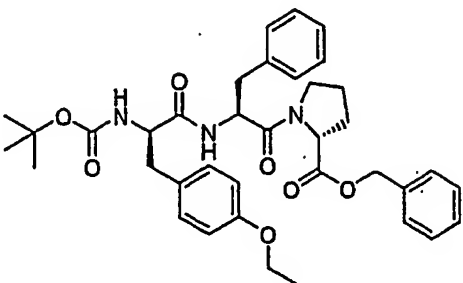
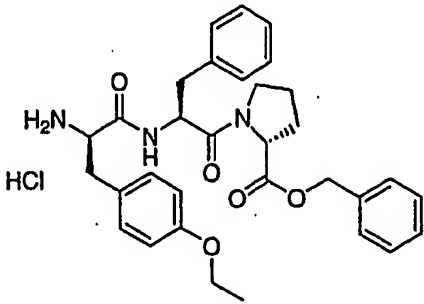
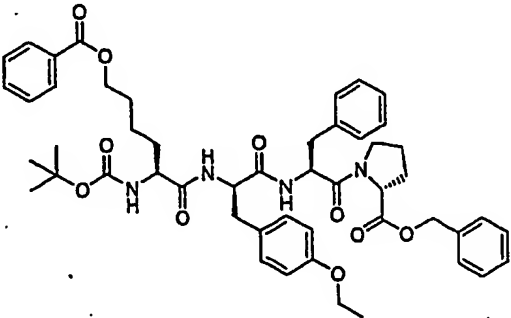
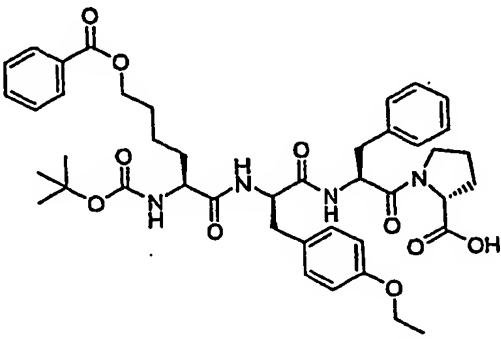
Compound (526)	Compound (527)
	
Compound (528)	Compound (529)
	
Compound (530)	Compound (531)
	
Compound (532)	Compound (533)
	

Table 2-67

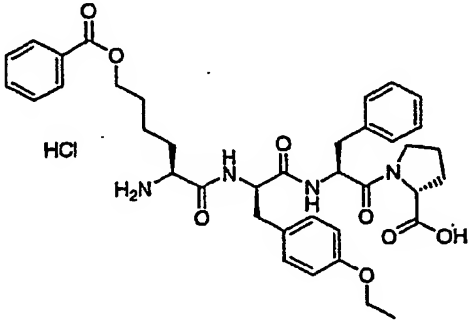
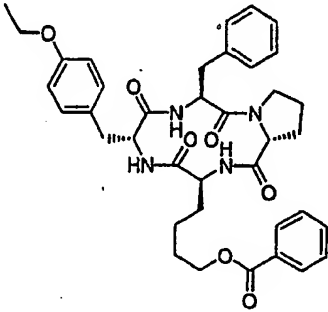
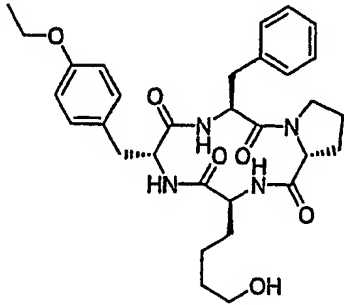
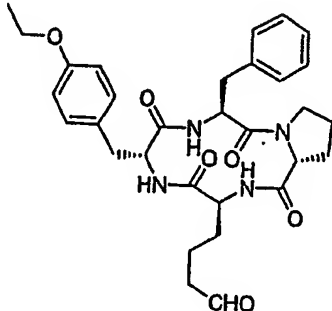
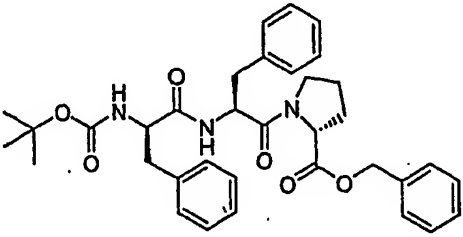
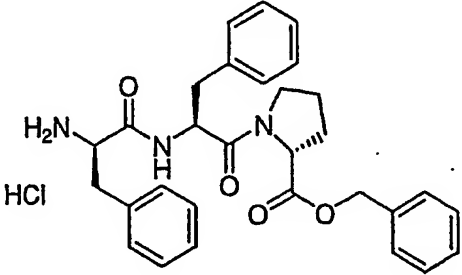
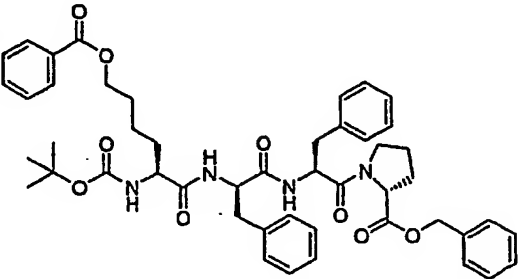
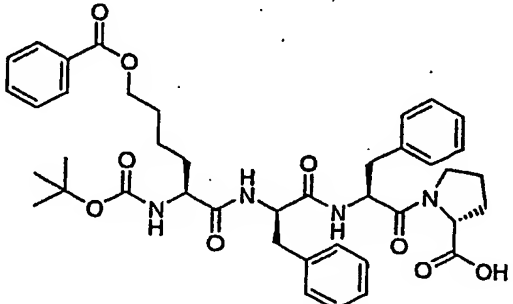
Compound (534)	Compound (535)
	
Compound (536)	Compound (537)
	
Compound (538)	Compound (539)
	
Compound (540)	Compound (541)
	

Table 2-68

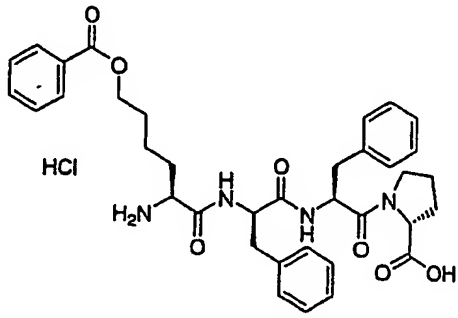
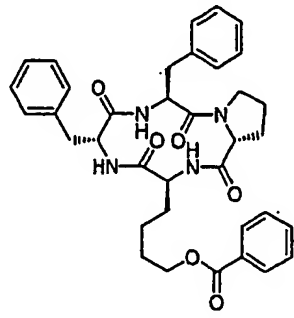
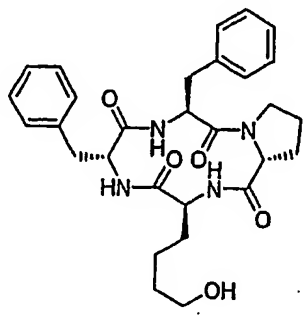
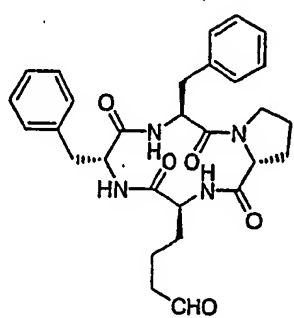
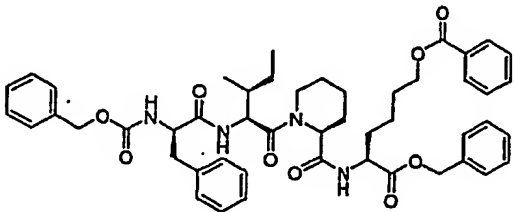
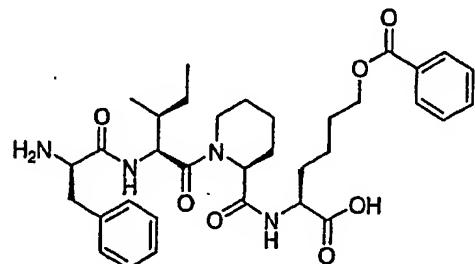
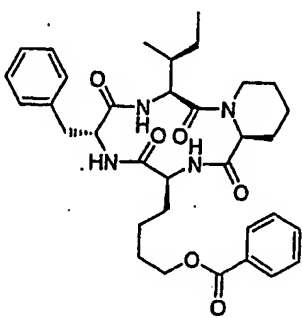
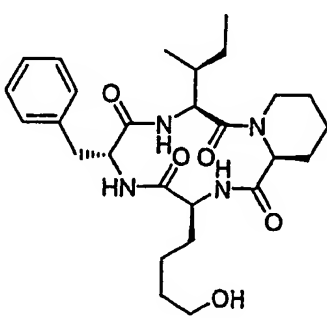
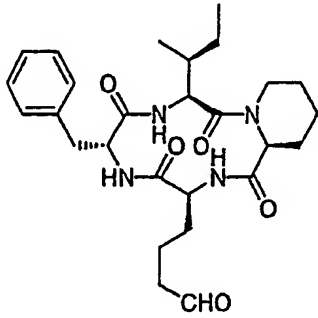
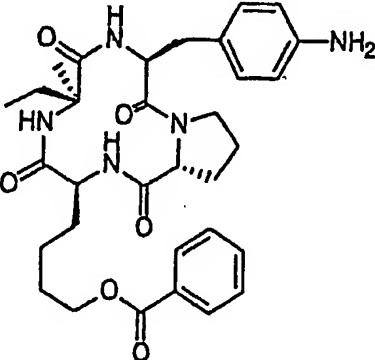
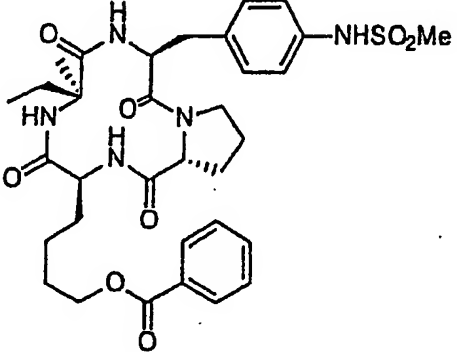
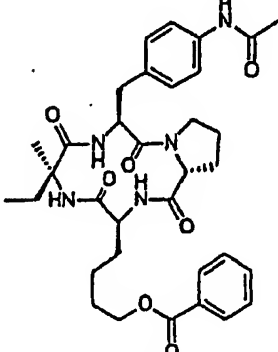
Compound (542)	Compound (543)
 HCl	
Compound (544)	Compound (545)
	
Compound (546)	Compound (547)
	
Compound (548)	Compound (549)
	

Table 2-69

Compound (550)	Compound (551)
	
Compound (552)	Compound (553)
	

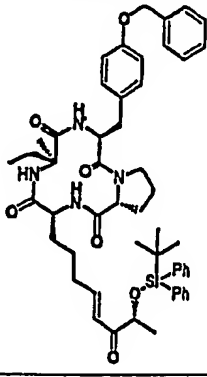
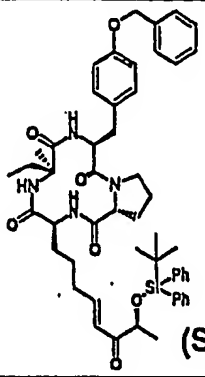
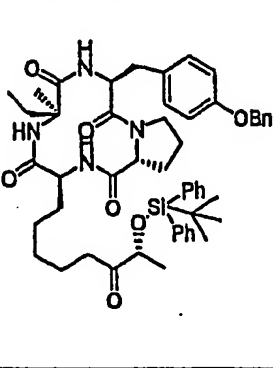
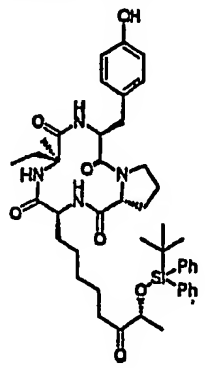
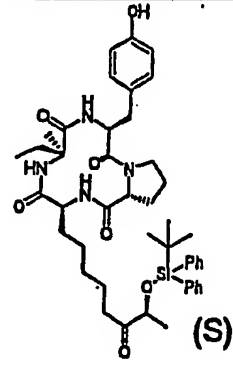
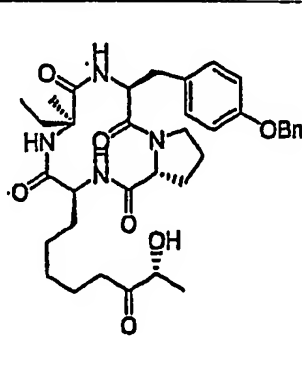
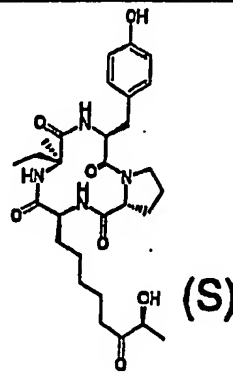
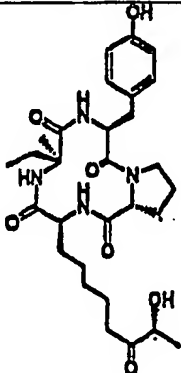
Compound E1	Compound E2
	 (S)
Compound E3	Compound E4
	
Compound E5	Compound E6
 (S)	
Compound E7	Compound E8
 (S)	 (R)

Table 2-71

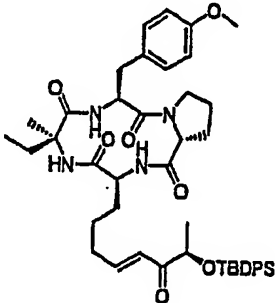
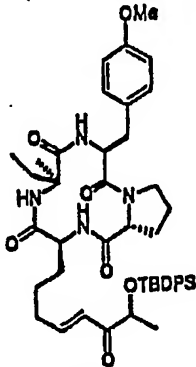
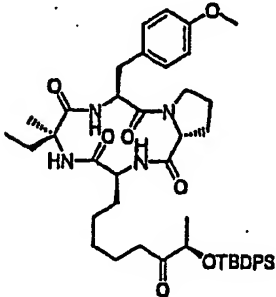
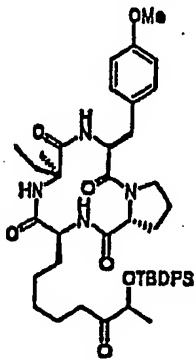
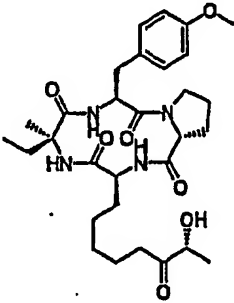
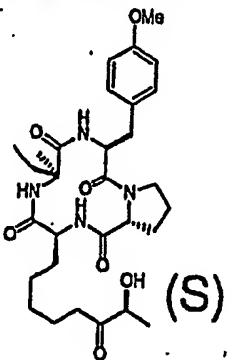
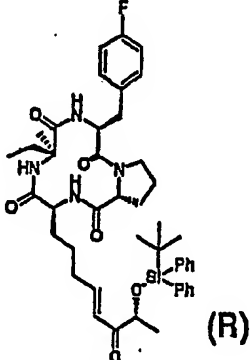
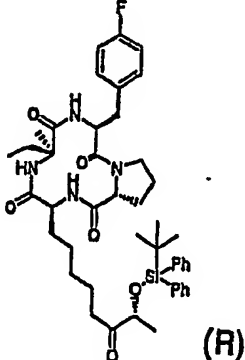
Compound E9	Compound E10
	
Compound E11	Compound E12
	
Compound E13	Compound E14
	
Compound E15	Compound E16
	

Table 2-72

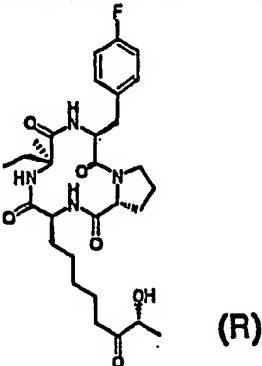
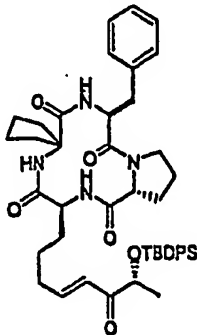
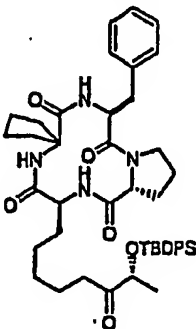
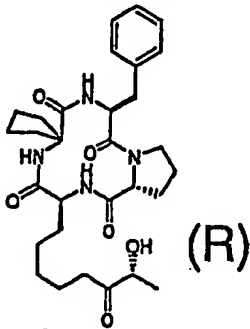
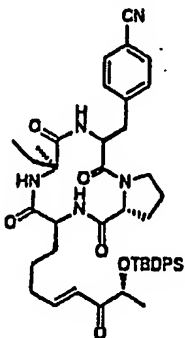
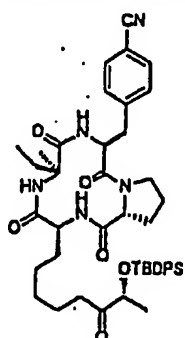
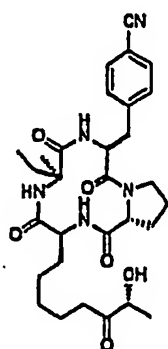
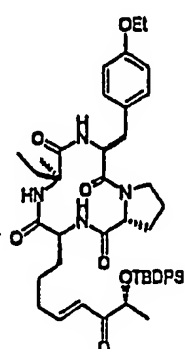
Compound E17	Compound E18
 (R)	
Compound E19	Compound E20
	
Compound E21	Compound E22
	
Compound E23	Compound E24
	

Table 2-73

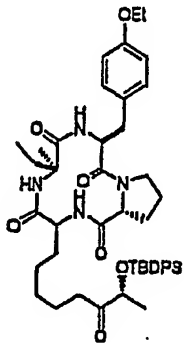
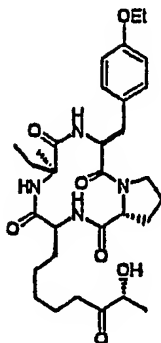
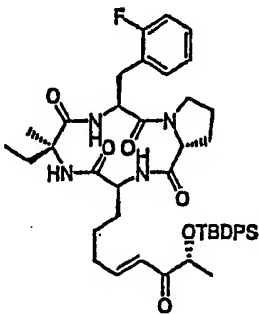
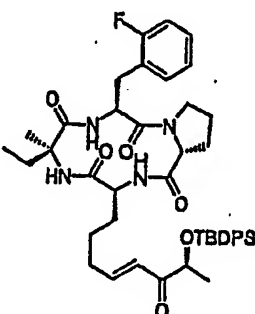
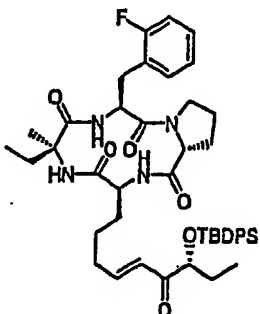
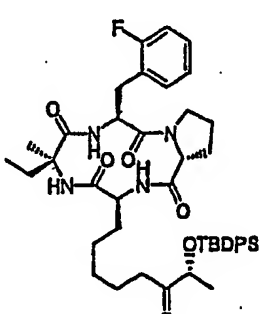
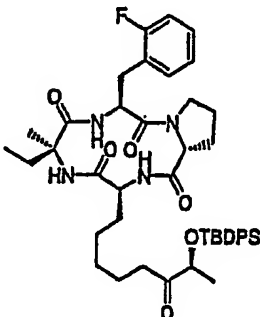
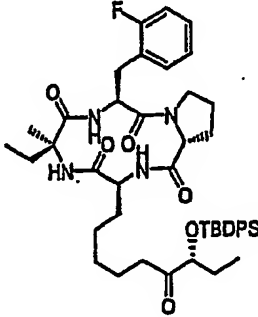
Compound E25	Compound E26
	
Compound E27	Compound E28
	
Compound E29	Compound E30
	
Compound E31	Compound E32
	

Table 2-74

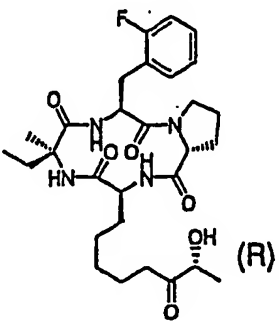
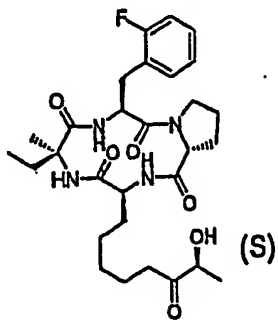
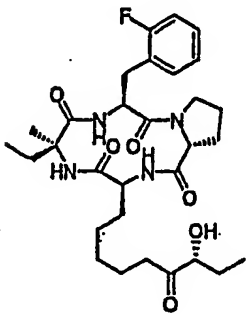
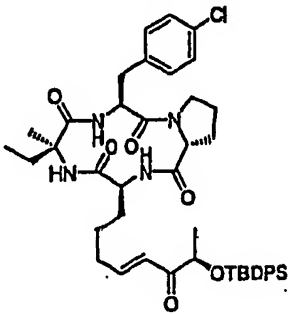
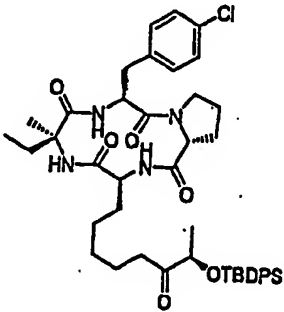
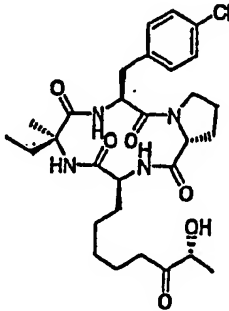
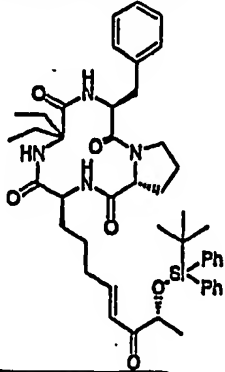
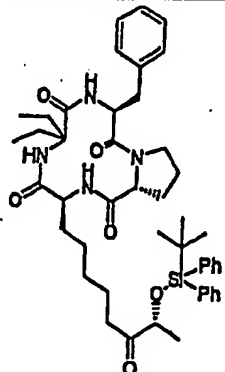
Compound E33	Compound E34
 (R)	 (S)
Compound E35	Compound E36
	
Compound E37	Compound E38
	
Compound E39	Compound E40
	

Table 2-75

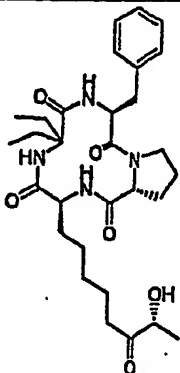
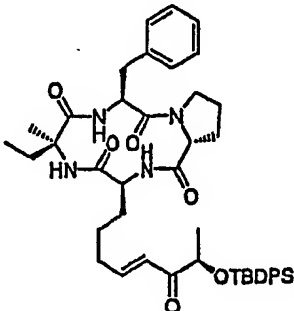
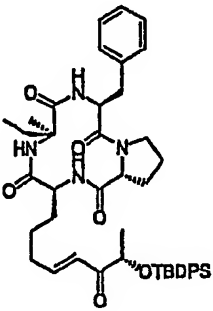
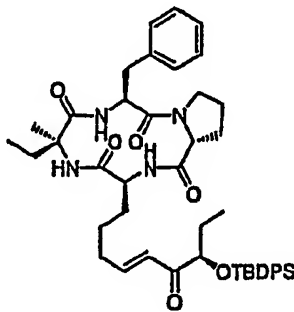
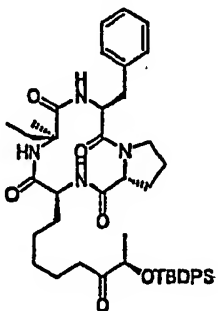
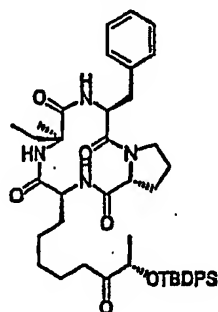
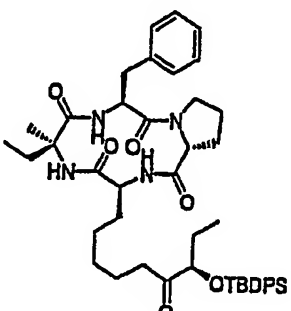
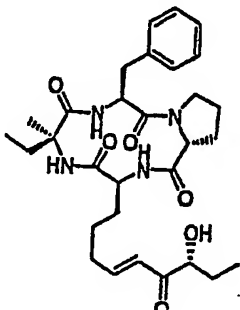
Compound E41	Compound E42
	
Compound E43	Compound E44
	
Compound E45	Compound E46
	
Compound E47	Compound E48
	

Table 2-76

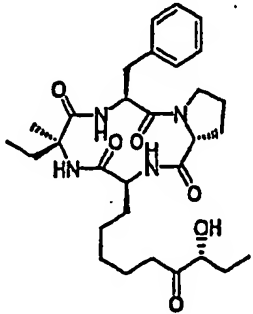
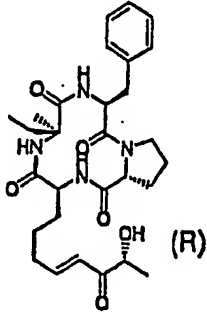
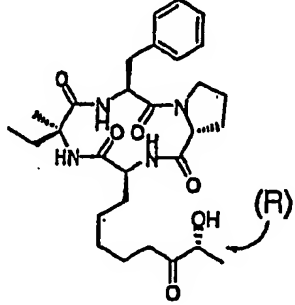
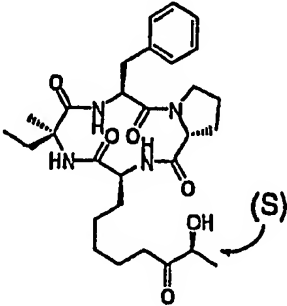
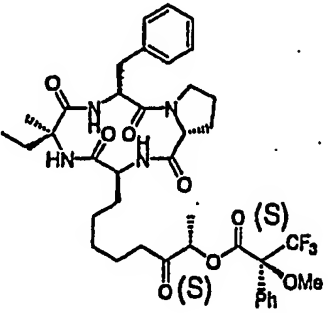
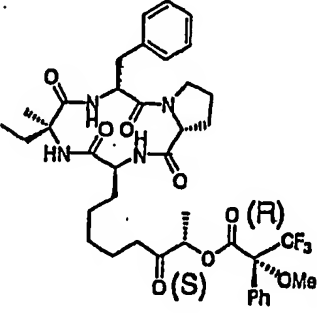
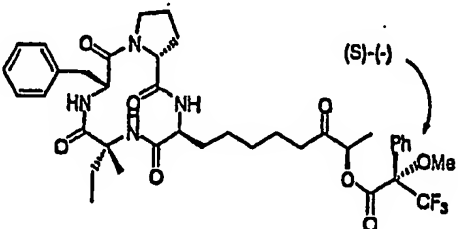
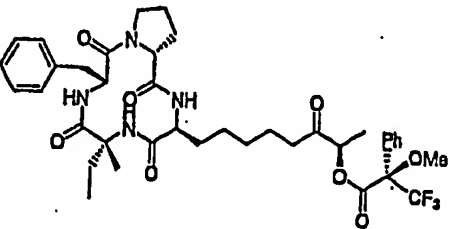
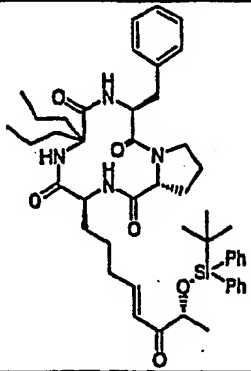
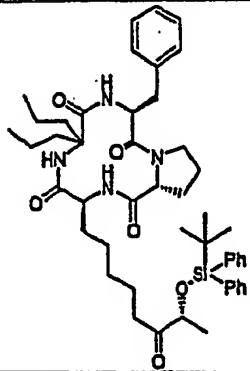
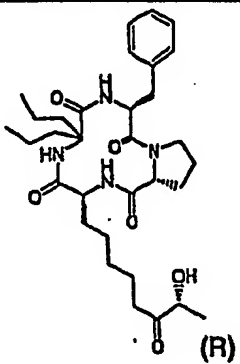
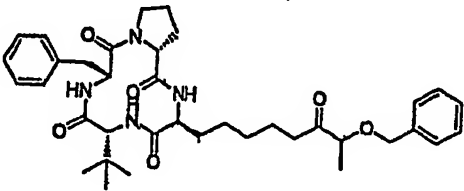
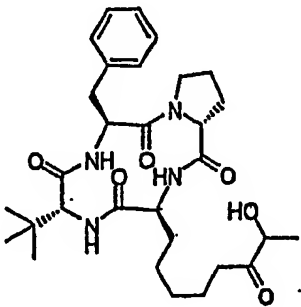
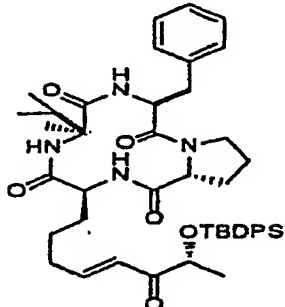
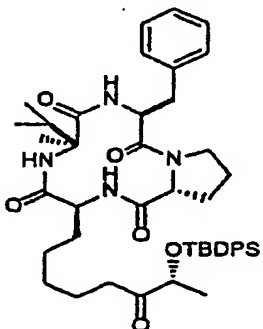
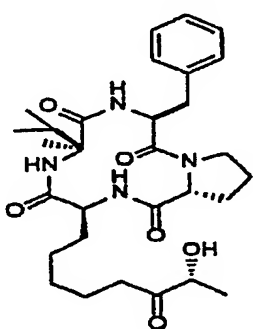
Compound E49	Compound E50
	
Compound E51	Compound E52
	
Compound E53	Compound E54
	
Compound E55	Compound E56
	

Table 2-77

Compound E57	Compound E58
	
Compound E59	Compound E60
	
Compound E61	Compound E62
	
Compound E63	Compound E64
	

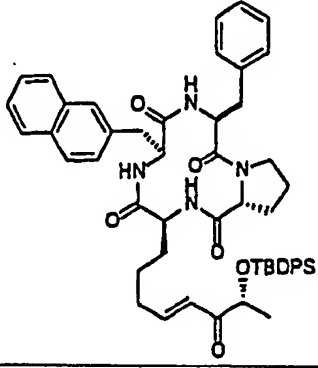
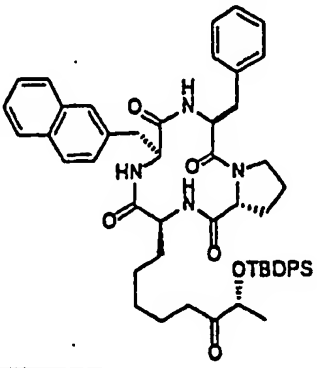
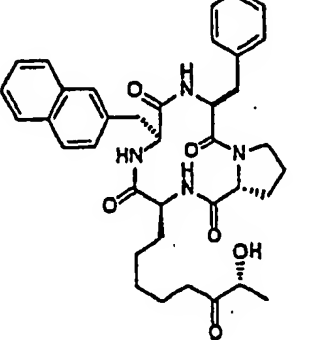
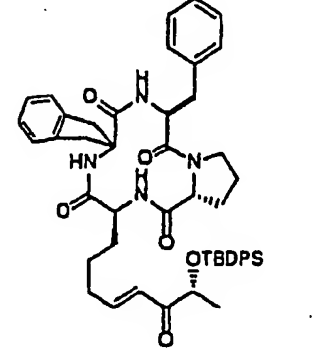
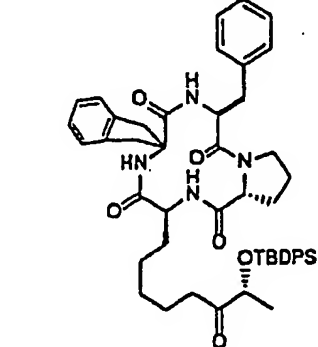
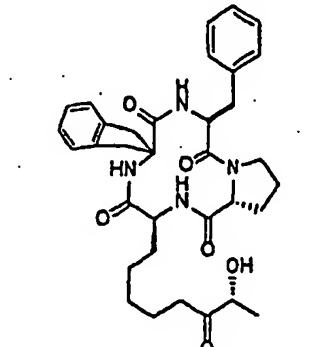
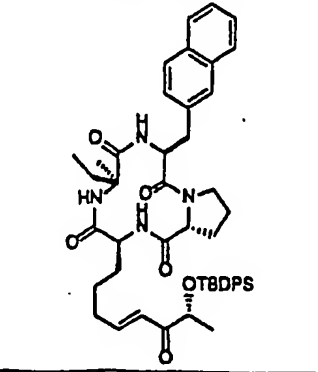
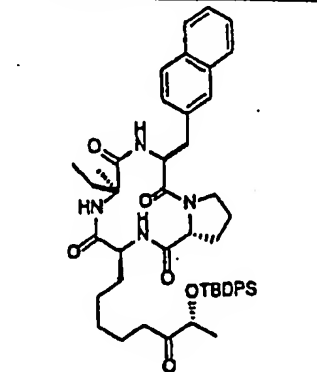
Compound E65	Compound E66
	
Compound E67	Compound E68
	
Compound E69	Compound E70
	
Compound E71	Compound E72
	

Table 2-79

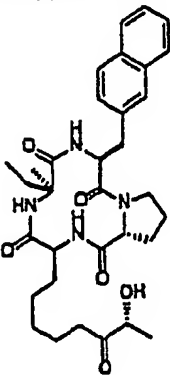
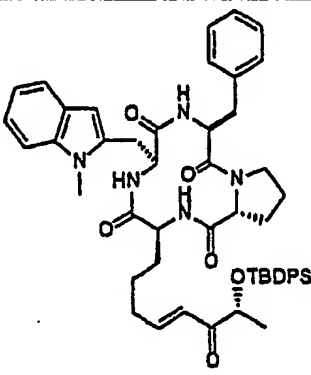
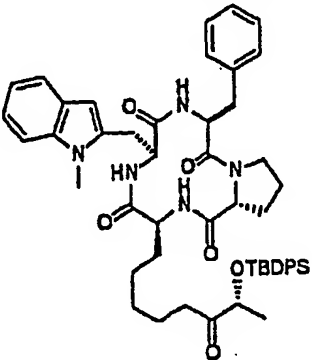
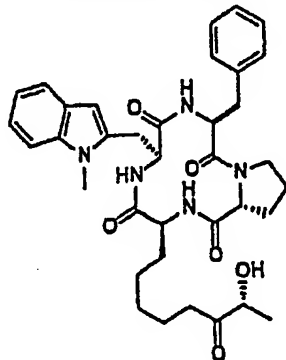
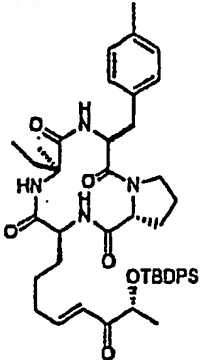
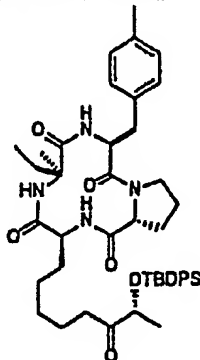
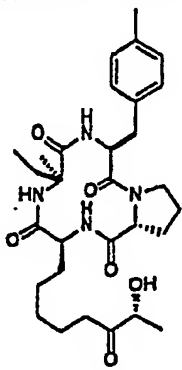
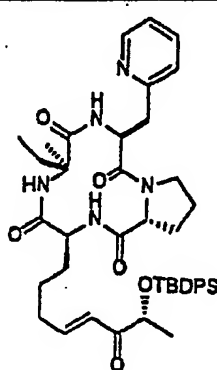
Compound E73	Compound E74
	
Compound E75	Compound E76
	
Compound E77	Compound E78
	
Compound E79	Compound E80
	

Table 2-80

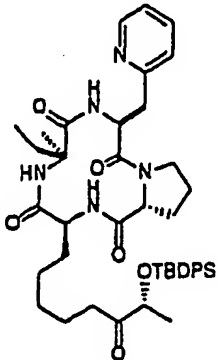
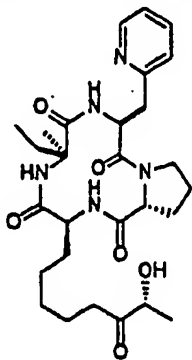
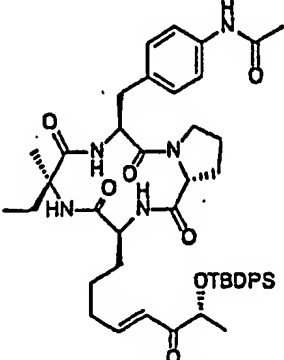
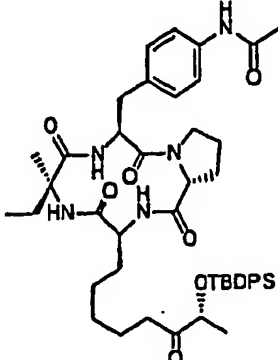
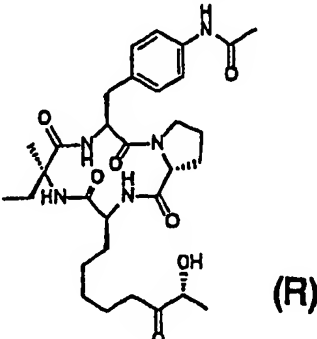
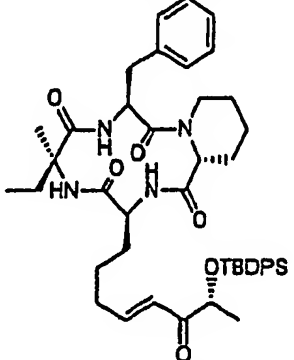
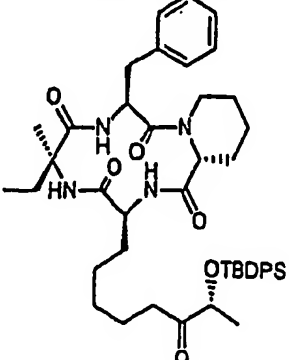
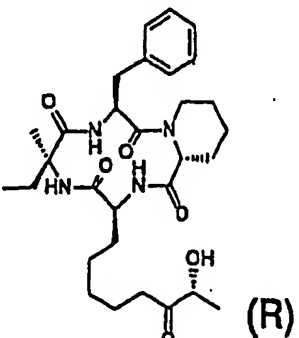
Compound E81	Compound E82
	
Compound E83	Compound E84
	
Compound E85	Compound E86
 (R)	
Compound E87	Compound E88
	 (R)

Table 2-81

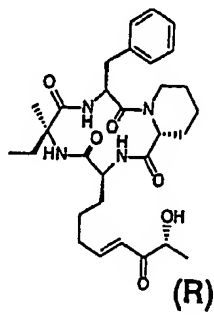
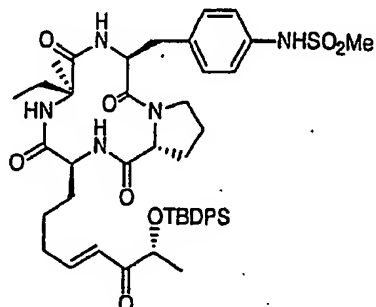
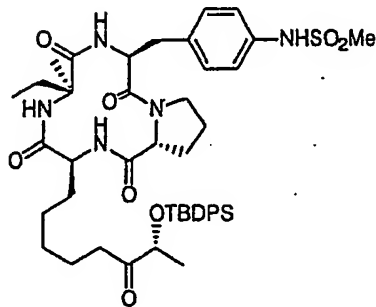
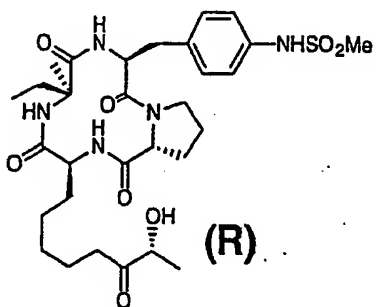
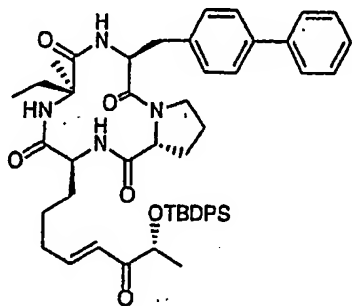
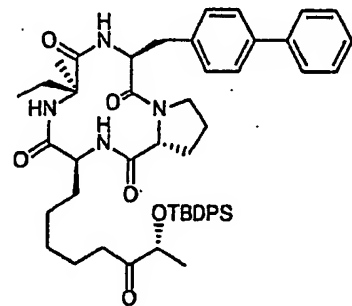
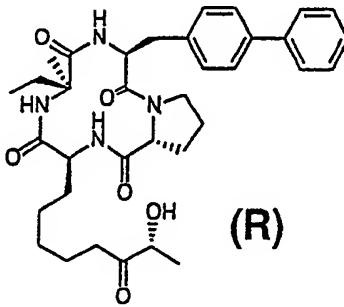
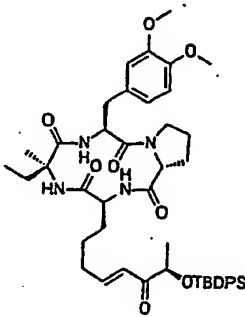
Compound E89	Compound E90
 (R)	
Compound E91	Compound E92
	 (R)
Compound E93	Compound E94
	
Compound E95	Compound E96
 (R)	

Table 2-82

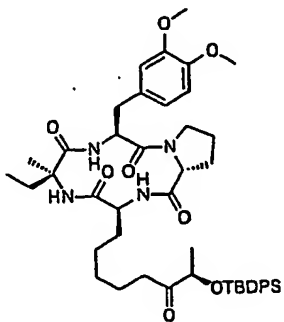
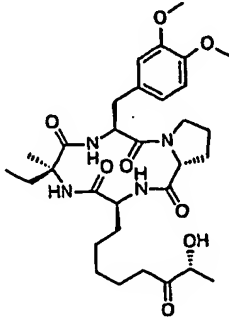
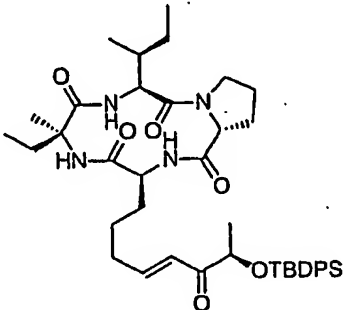
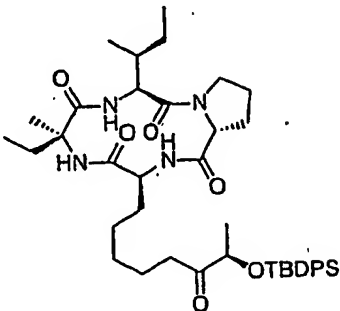
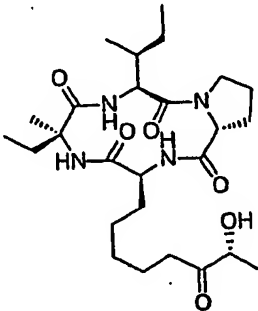
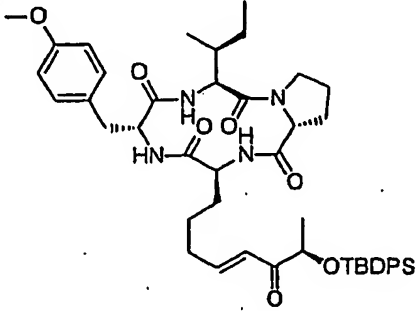
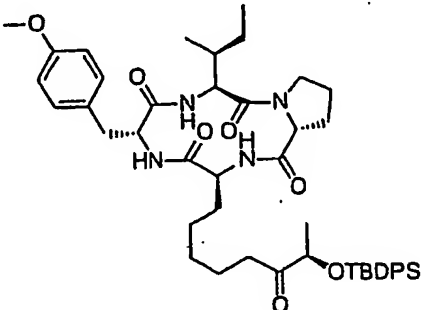
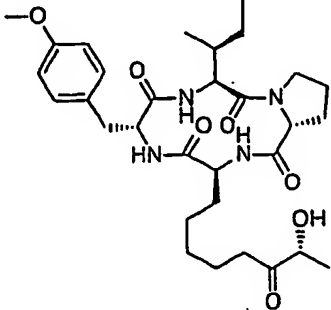
Compound E97	Compound E98
	
Compound E99	Compound E100
	
Compound E101	Compound E102
	
Compound E103	Compound E104
	

Table 2-83

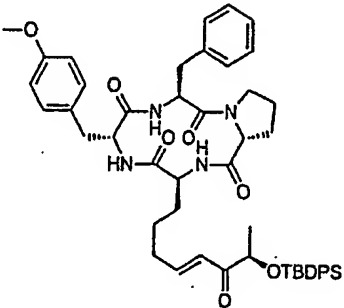
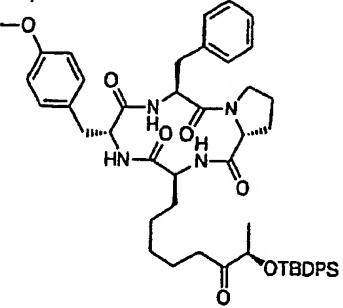
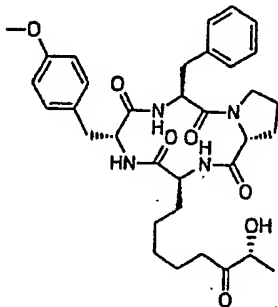
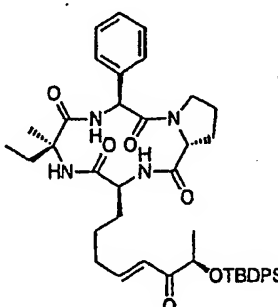
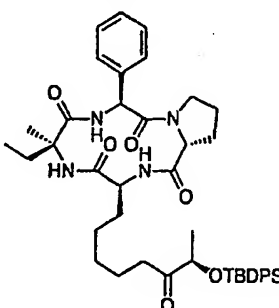
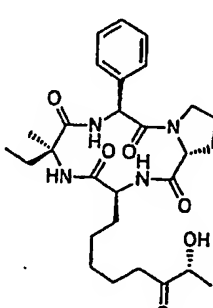
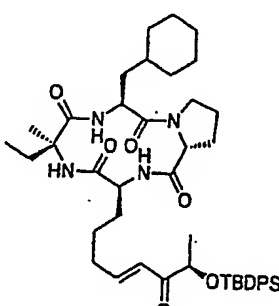
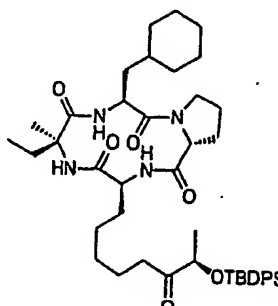
Compound E105	Compound E106
	
Compound E107	Compound E108
	
Compound E109	Compound E110
	
Compound E111	Compound E112
	

Table 2-84

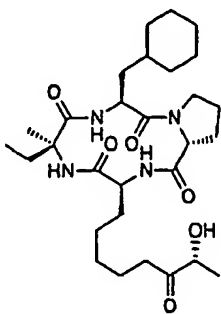
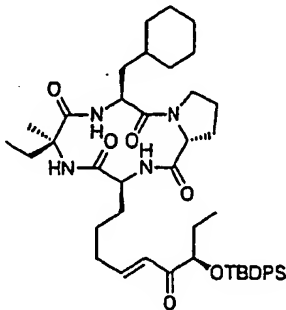
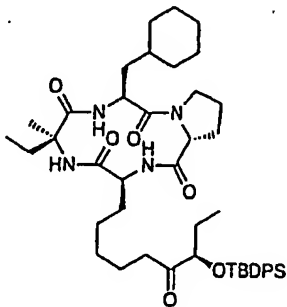
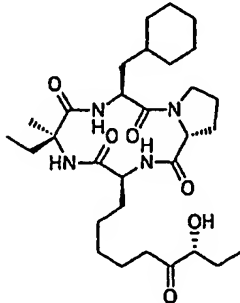
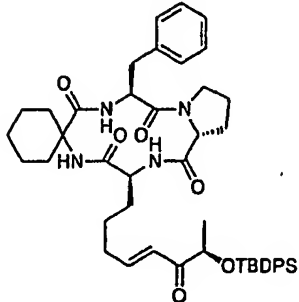
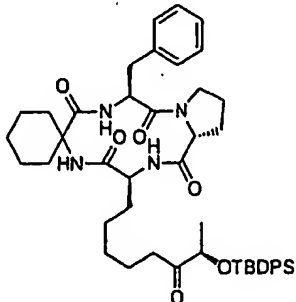
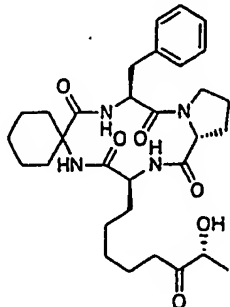
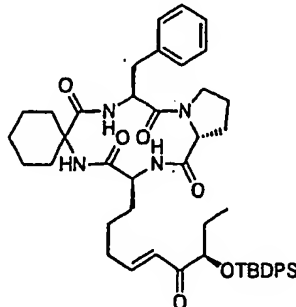
Compound E113	Compound E114
	
Compound E115	Compound E116
	
Compound E117	Compound E118
	
Compound E119	Compound E120
	

Table 2-85

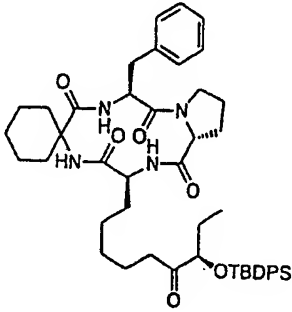
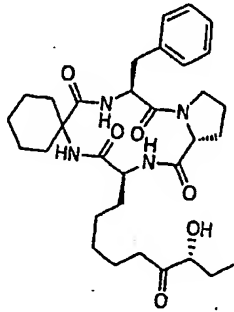
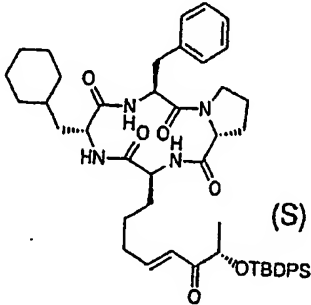
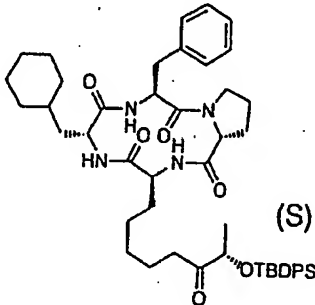
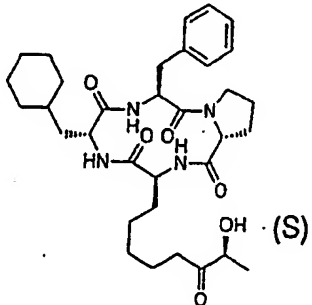
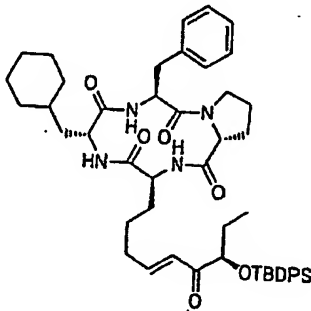
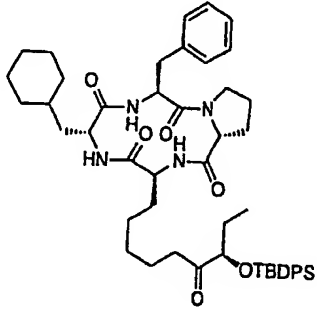
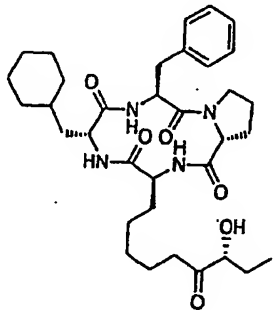
Compound E121	Compound E122
	
Compound E123	Compound E124
 (S)	 (S)
Compound E125	Compound E126
 (S)	
Compound E127	Compound E128
	

Table 2-86

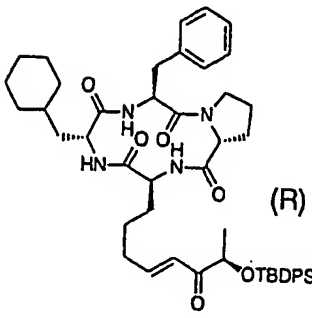
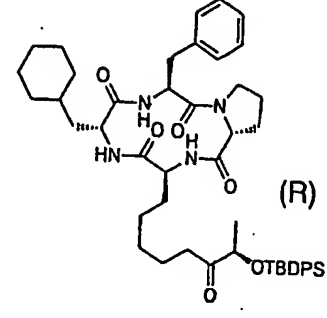
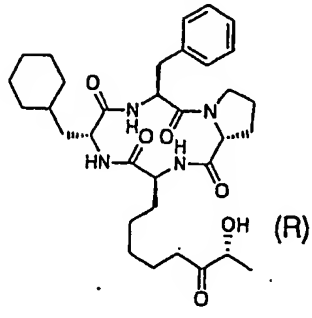
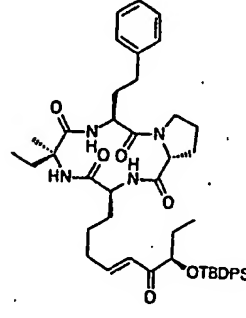
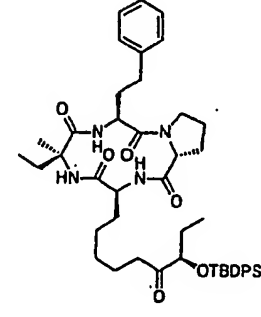
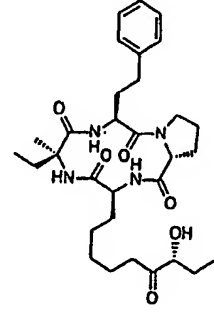
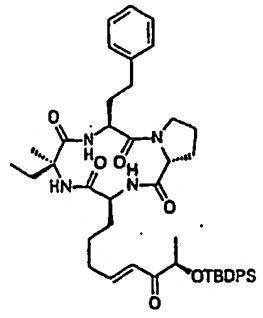
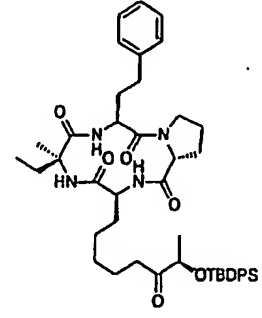
Compound E129	Compound E130
 (R)	 (R)
Compound E131	Compound E132
 (R)	
Compound E133	Compound E134
	
Compound E135	Compound E136
	

Table 2-87

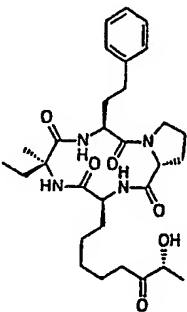
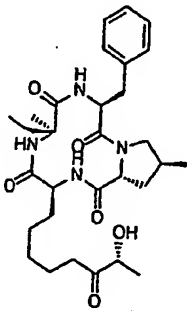
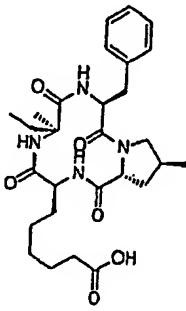
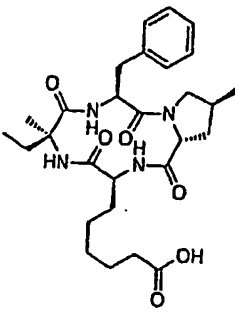
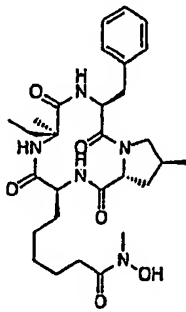
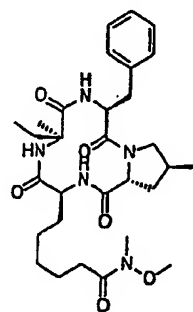
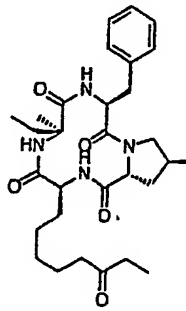
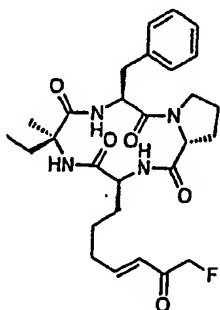
Compound E137	Compound E138
	
Compound E139	Compound E140
	
Compound E141	Compound E142
	
Compound E143	Compound E144
	

Table 2-88

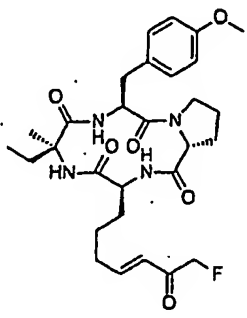
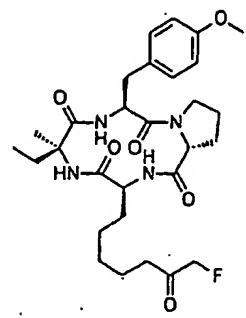
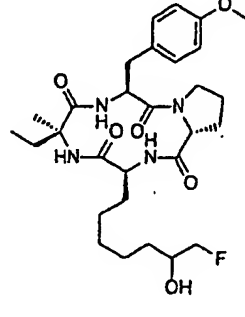
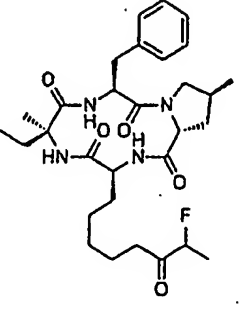
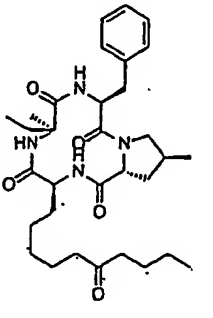
Compound E145	Compound E146
	
Compound E147	Compound E148
	
Compound E149	
	

Table 2-89

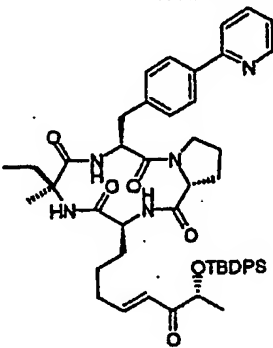
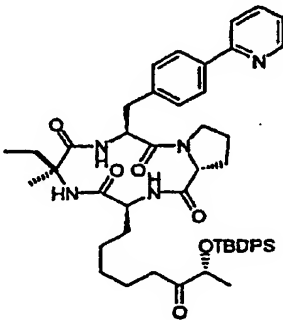
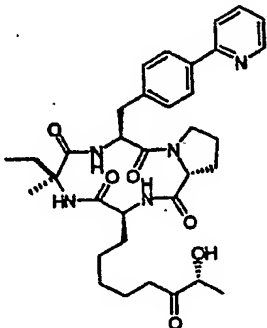
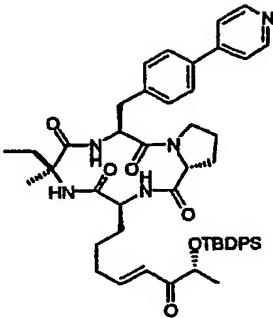
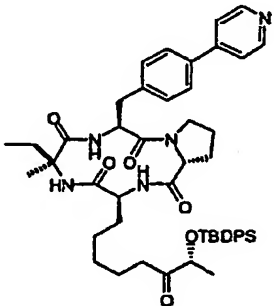
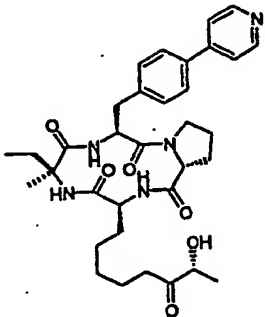
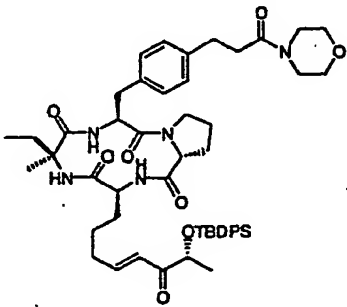
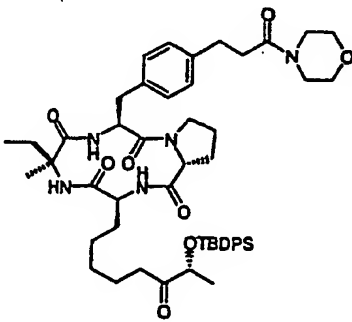
Compound E150	Compound E151
	
Compound E152	Compound E153
	
Compound E154	Compound E155
	
Compound E156	Compound E157
	

Table 2-90

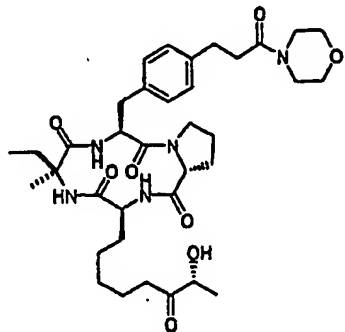
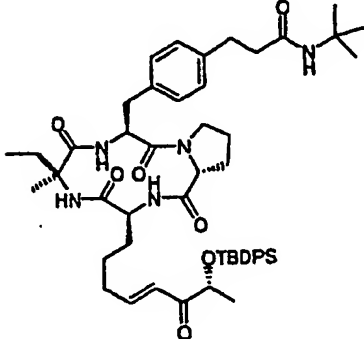
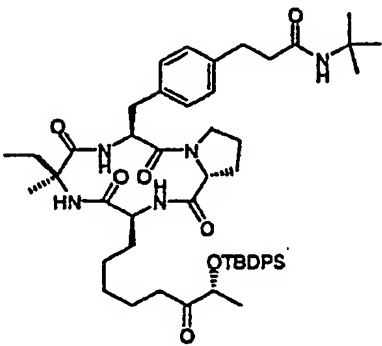
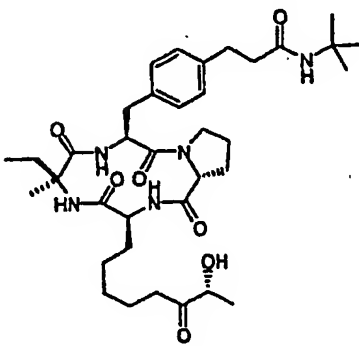
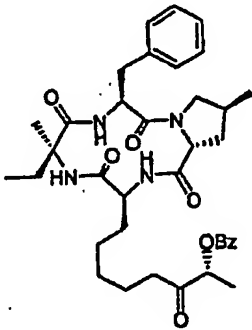
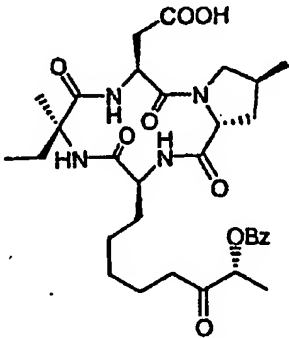
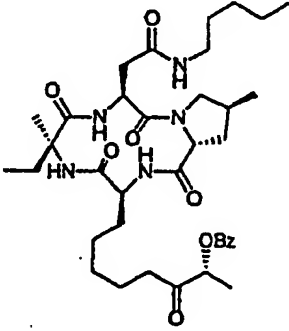
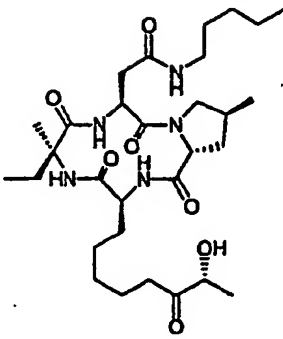
Compound E158	Compound E159
	
Compound E160	Compound E161
	
Compound E162	Compound E163
	
Compound E164	Compound E165
	

Table 2-91

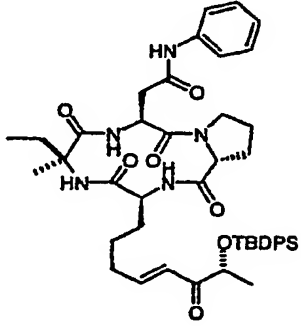
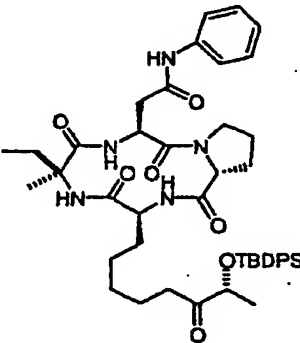
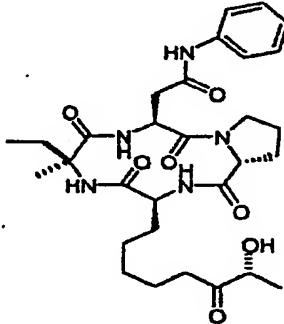
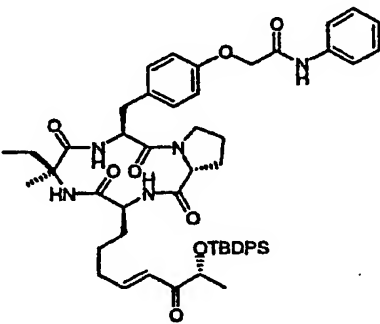
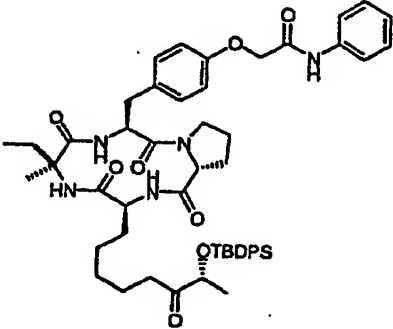
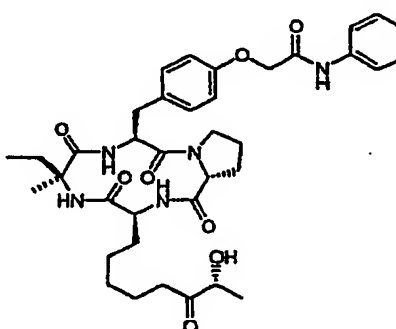
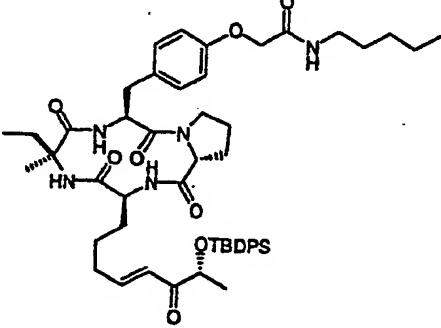
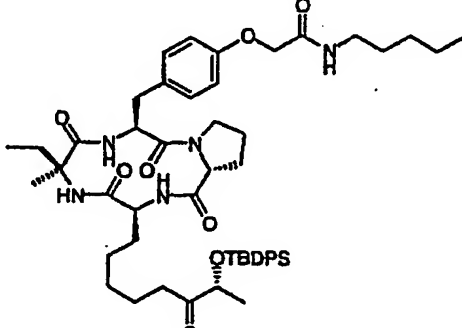
Compound E166	Compound E167
	
Compound E168	Compound E169
	
Compound E170	Compound E171
	
Compound E172	Compound E173
	

Table 2-92

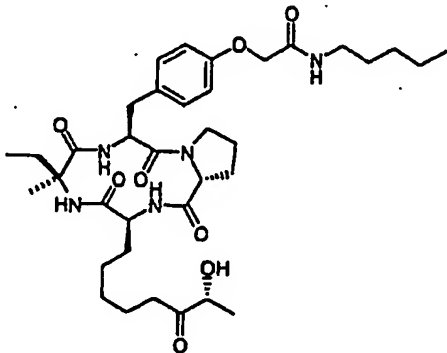
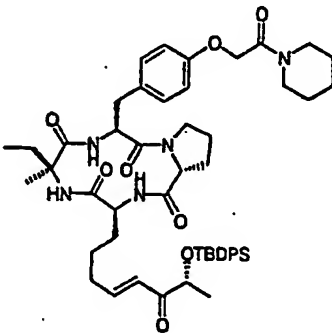
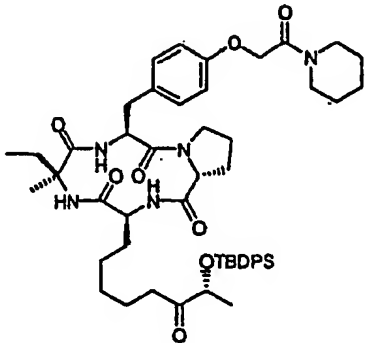
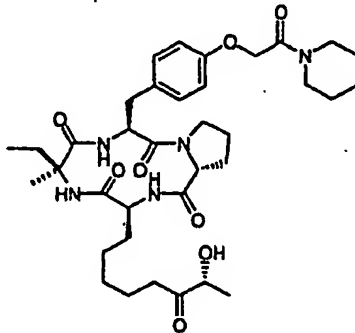
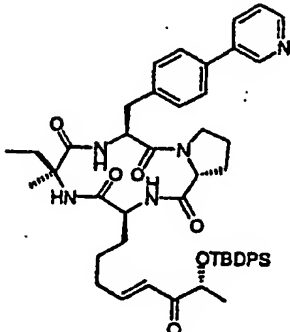
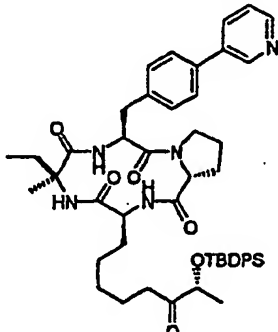
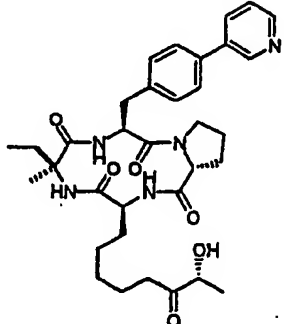
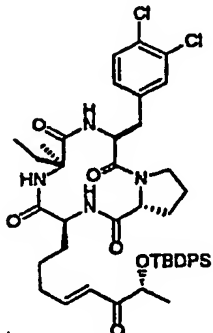
Compound E174	Compound E175
	
Compound E176	Compound E177
	
Compound E178	Compound E179
	
Compound E180	Compound E181
	

Table 2-93

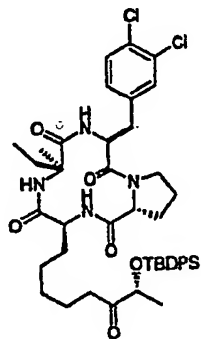
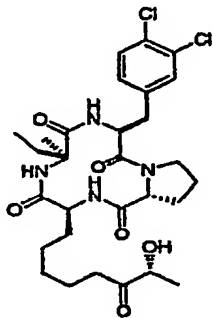
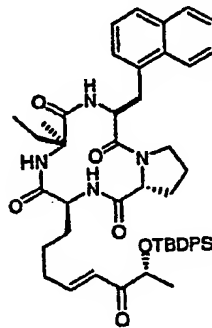
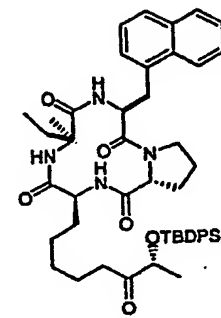
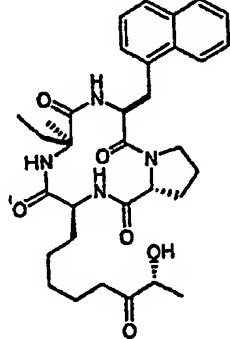
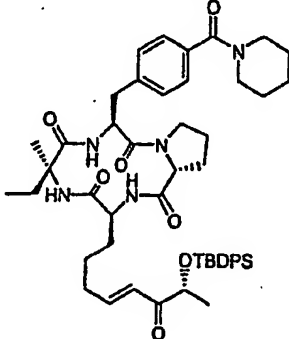
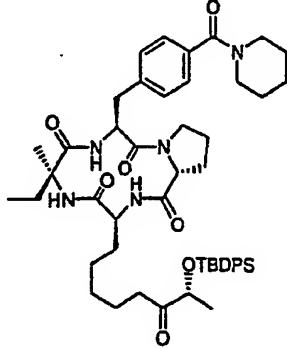
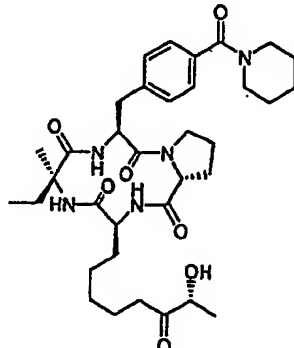
Compound E182	Compound E183
	
Compound E184	Compound E185
	
Compound E186	Compound E187
	
Compound E188	Compound E189
	

Table 2-94

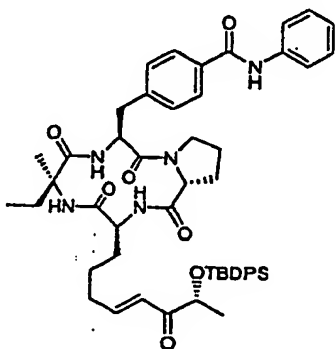
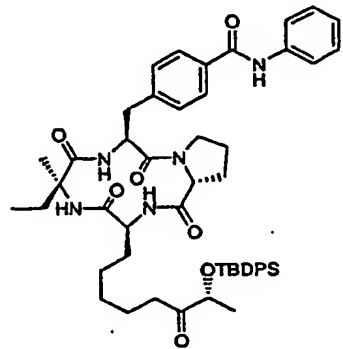
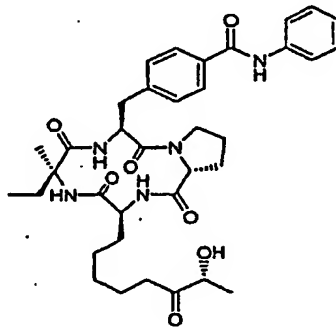
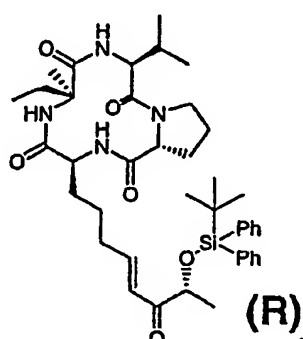
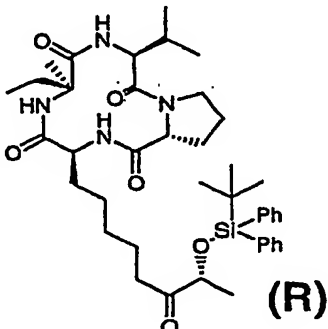
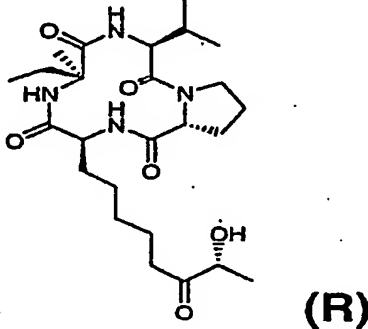
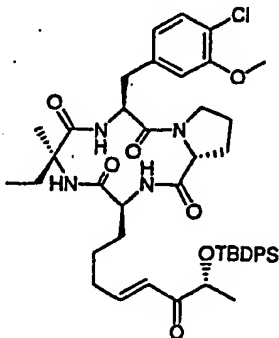
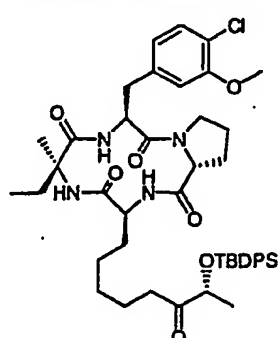
Compound E190	Compound E191
	
Compound E192	Compound E193
	
Compound E194	Compound E195
	
Compound E196	Compound E197
	

Table 2-95

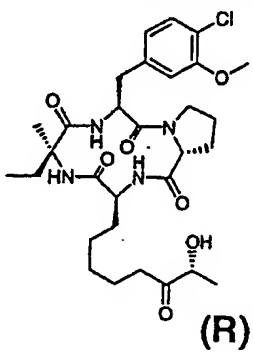
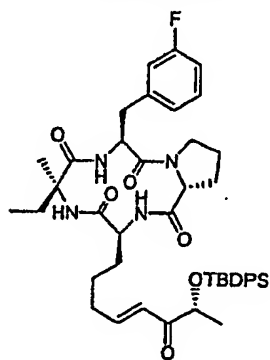
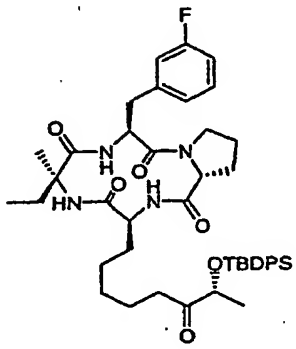
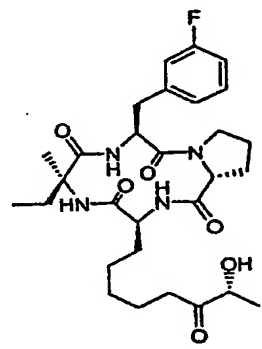
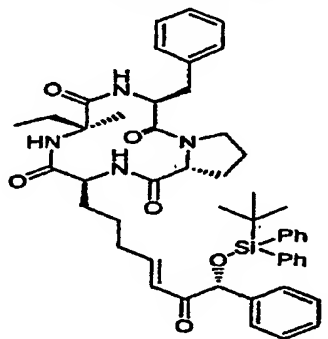
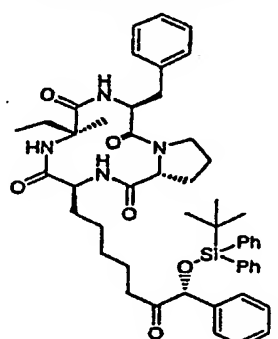
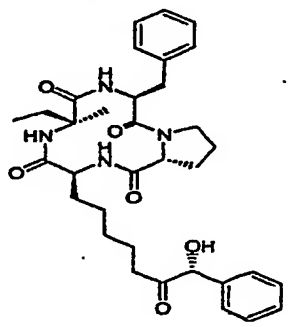
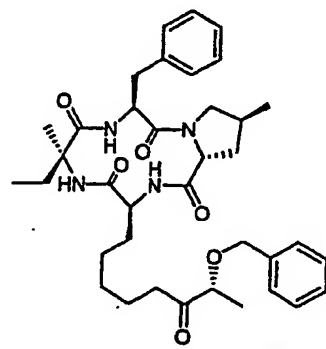
Compound E198	Compound E199
 (R)	
Compound E200	Compound E201
	
Compound E202	Compound E203
	
Compound E204	Compound E205
	

Table 2-96

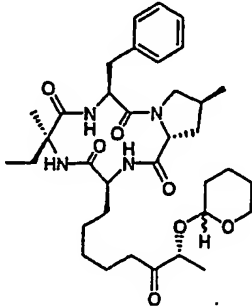
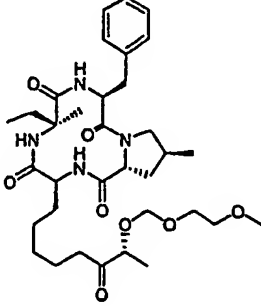
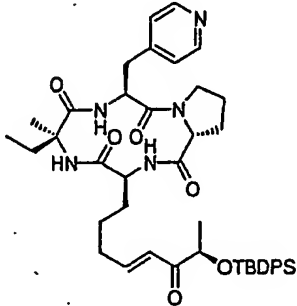
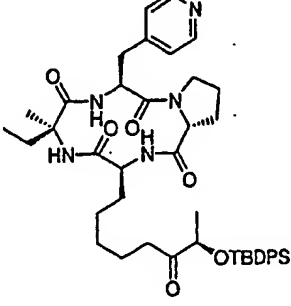
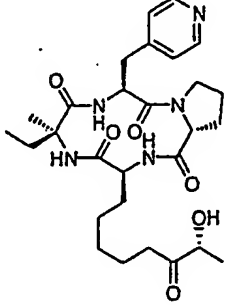
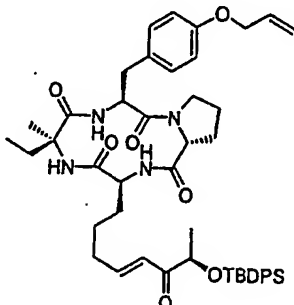
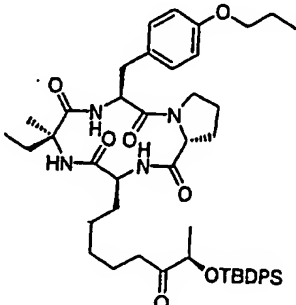
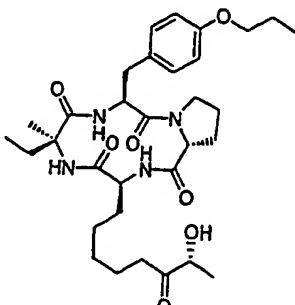
Compound E206	Compound E207
	
Compound E208	Compound E209
	
Compound E210	Compound E211
	
Compound E212	Compound E213
	

Table 2-97

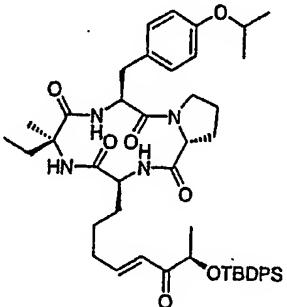
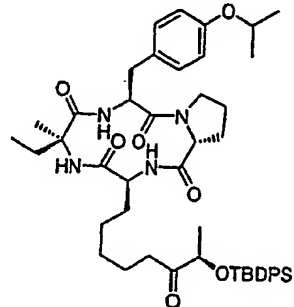
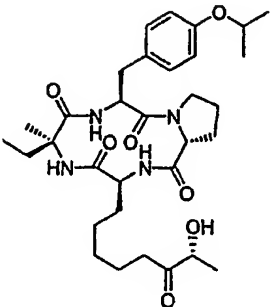
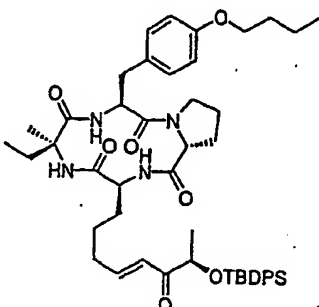
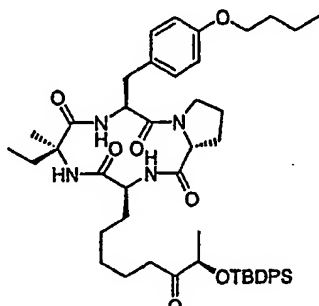
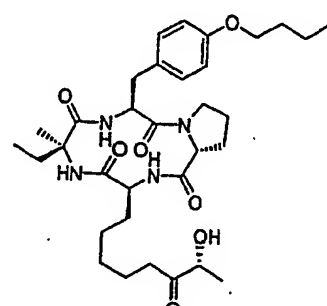
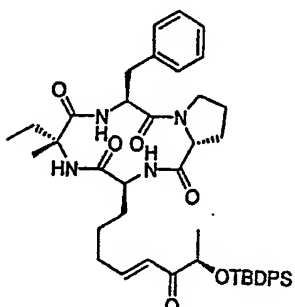
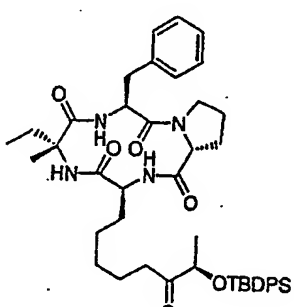
Compound E214	Compound E215
	
Compound E216	Compound E217
	
Compound E218	Compound E219
	
Compound E220	Compound E221
	

Table 2-98

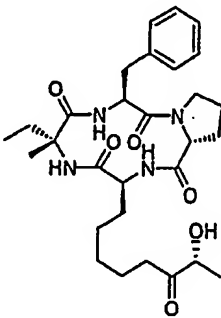
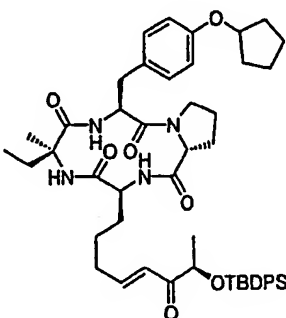
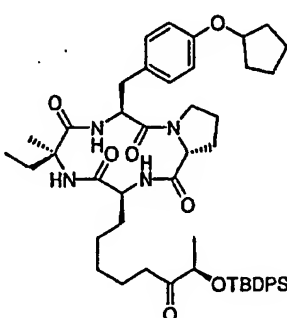
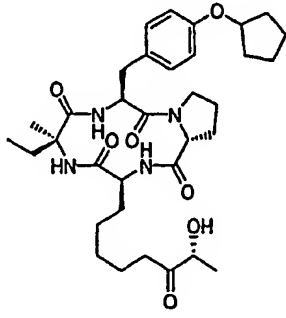
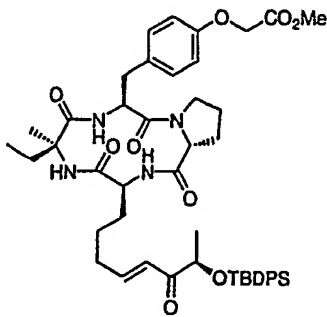
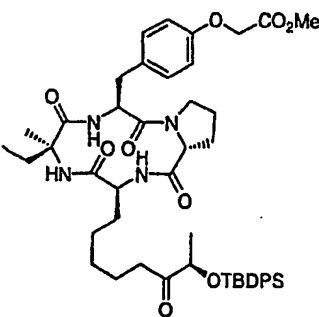
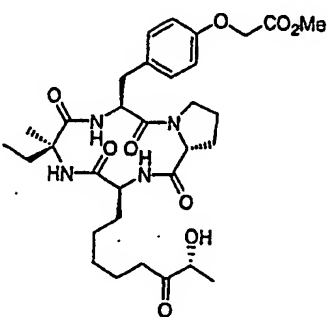
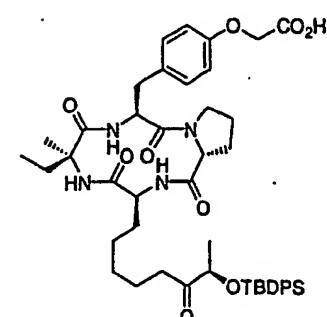
Compound E222	Compound E223
	
Compound E224	Compound E225
	
Compound E226	Compound E227
	
Compound E228	Compound E229
	

Table 2-99

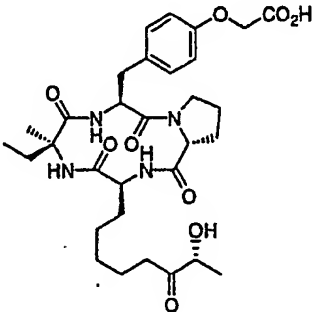
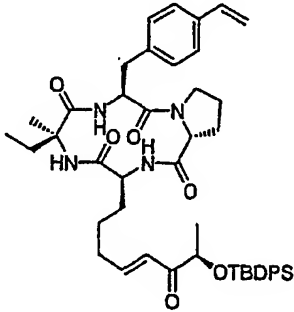
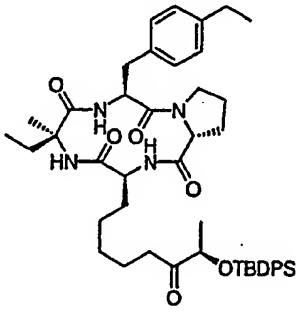
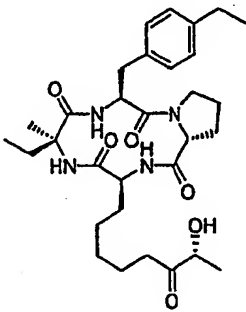
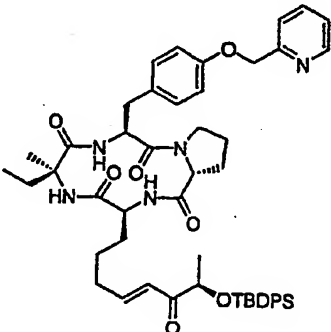
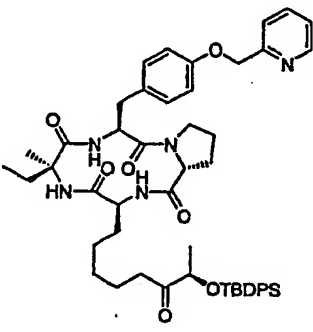
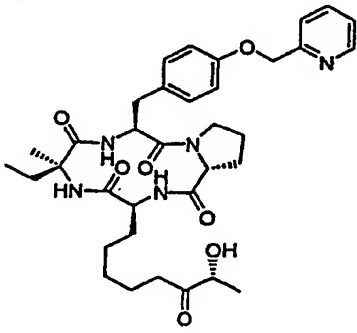
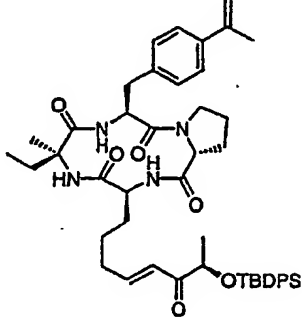
Compound E230	Compound E231
	
Compound E232	Compound E233
	
Compound E234	Compound E235
	
Compound E236	Compound E237
	

Table 2-100

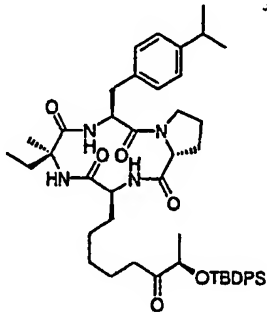
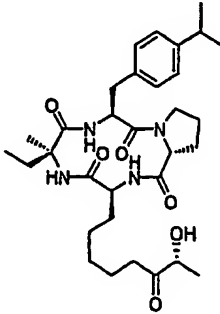
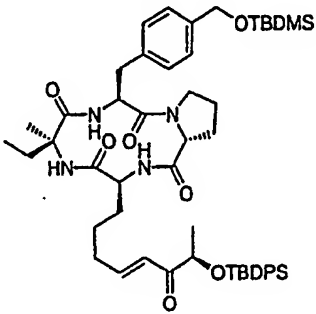
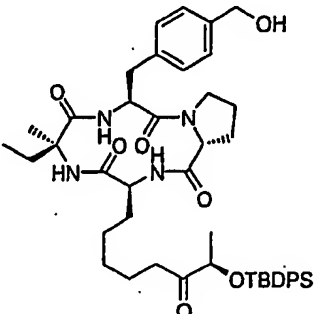
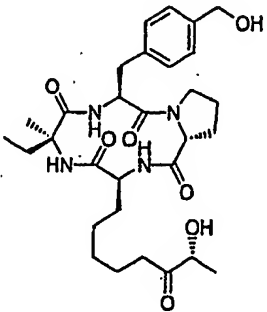
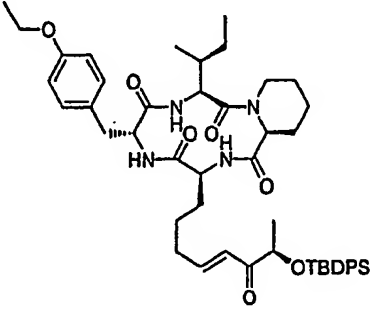
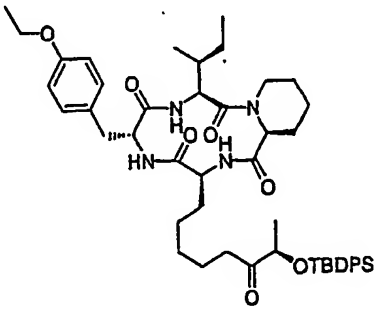
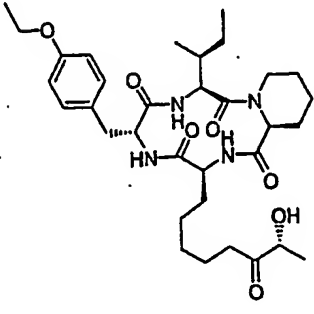
Compound E238	Compound E239
	
Compound E240	Compound E241
	
Compound E242	Compound E243
	
Compound E244	Compound E245
	

Table 2-101

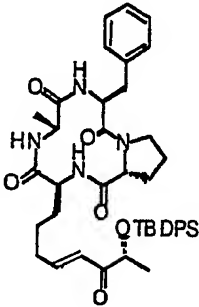
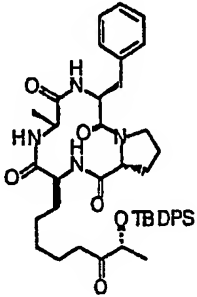
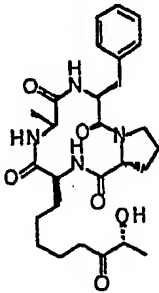
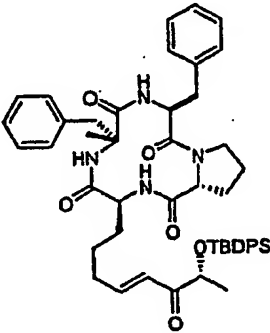
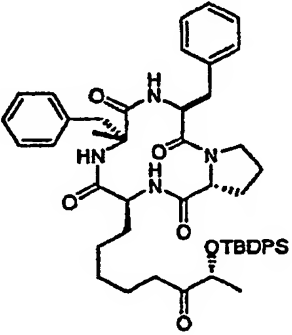
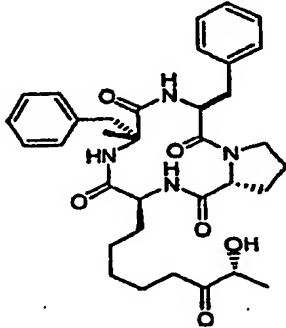
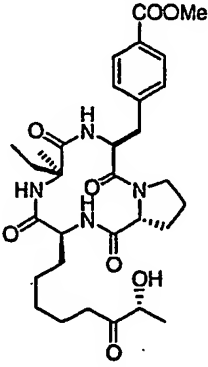
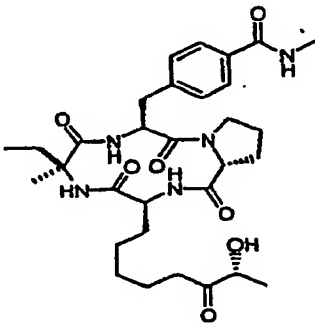
Compound E246	Compound E247
	
Compound E248	Compound E249
	
Compound E250	Compound E251
	
Compound E252	Compound E253
	

Table 2-102

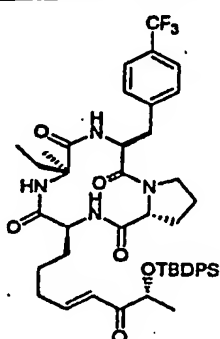
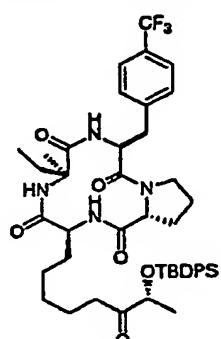
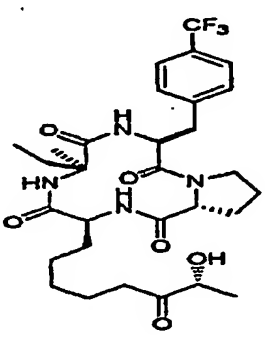
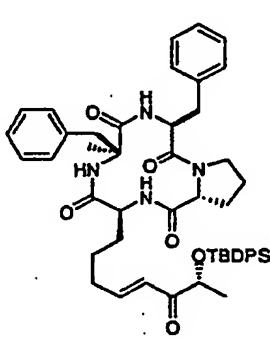
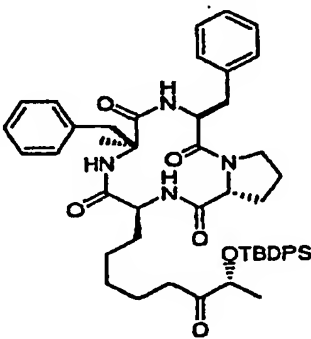
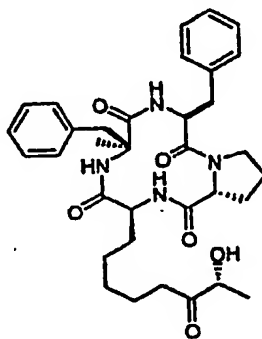
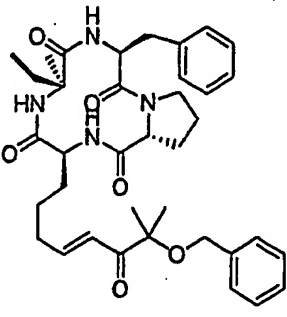
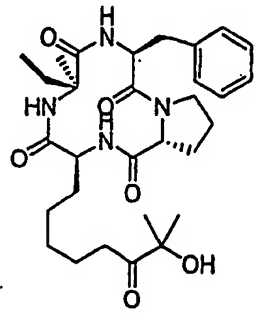
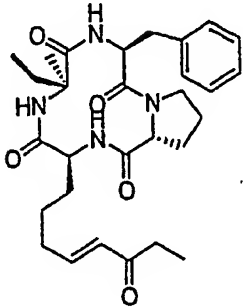
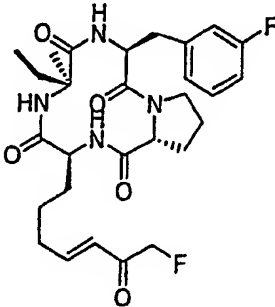
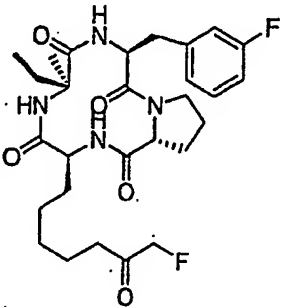
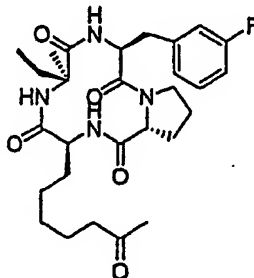
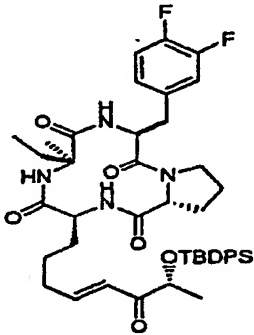
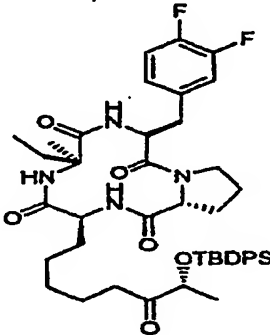
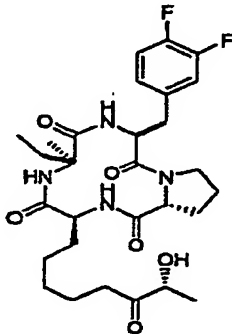
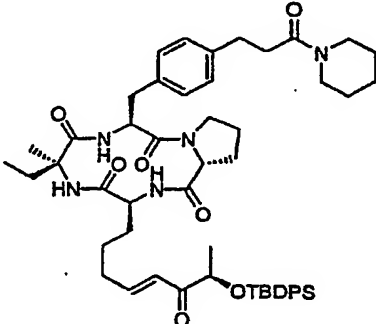
Compound E254	Compound E255
	
Compound E256	Compound E257
	
Compound E258	Compound E259
	
Compound E260	Compound E261
	

Table 2-103

Compound E262	Compound E263
	
Compound E264	Compound E265
	
Compound E266	Compound E267
	
Compound E268	Compound E269
	

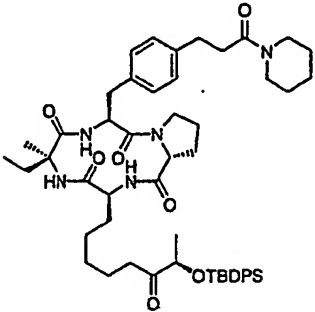
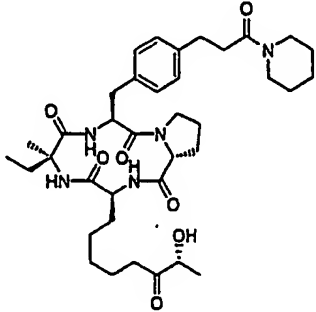
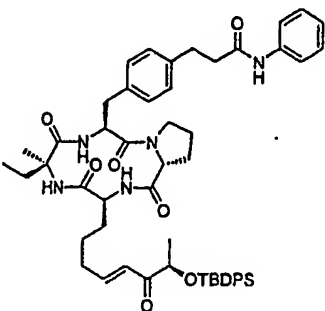
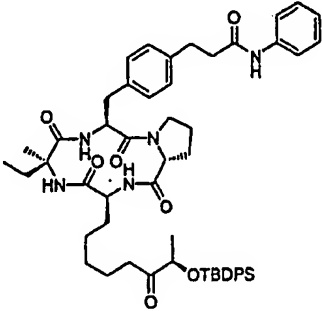
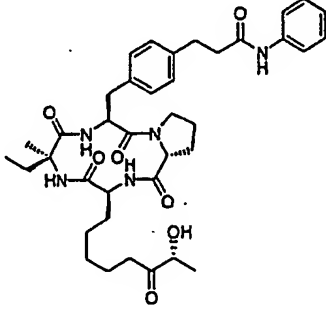
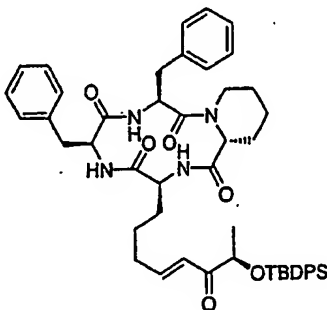
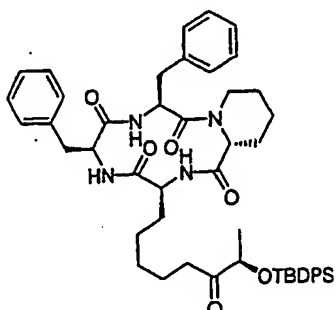
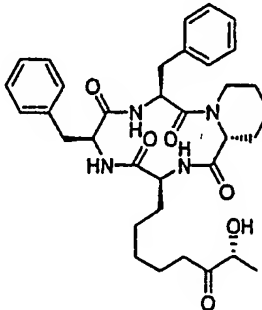
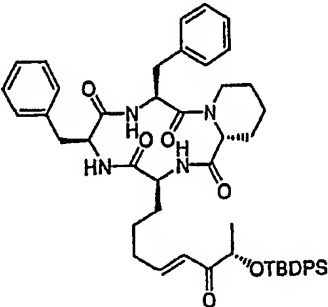
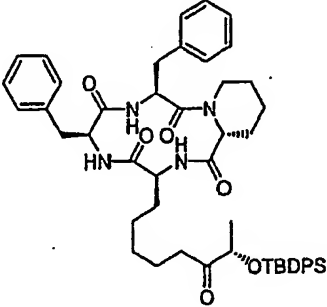
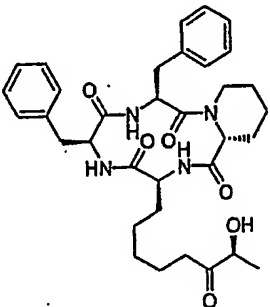
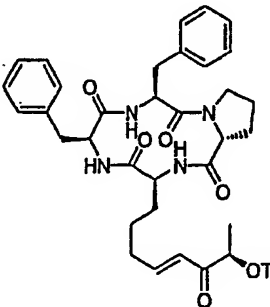
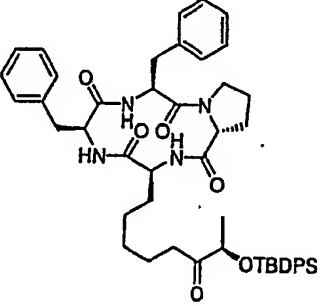
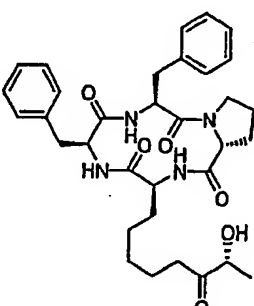
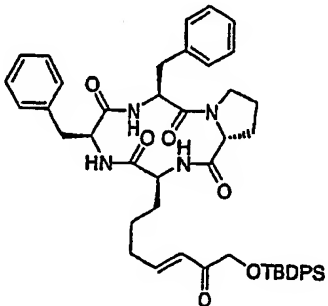
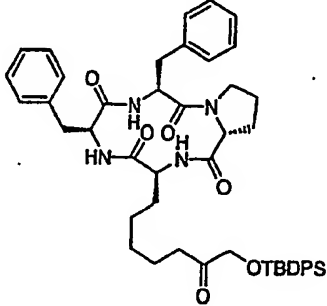
Compound E270	Compound E271
	
Compound E272	Compound E273
	
Compound E274	Compound E275
	
Compound E276	Compound E277
	

Table 2-105

Compound E278	Compound E279
	
Compound E280	Compound E281
	
Compound E282	Compound E283
	
Compound E284	Compound E285
	

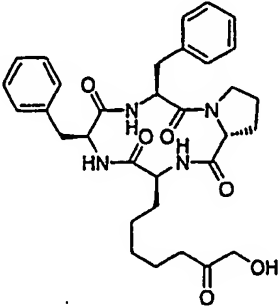
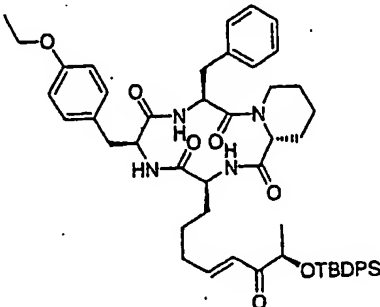
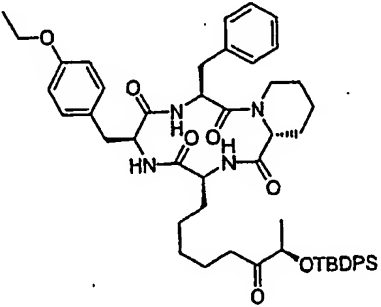
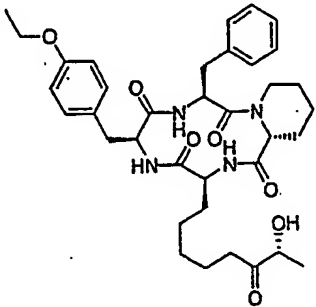
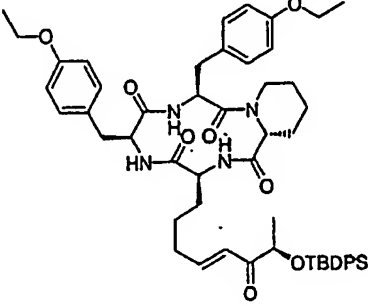
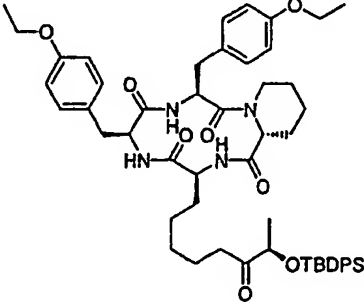
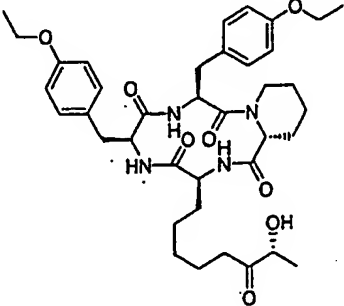
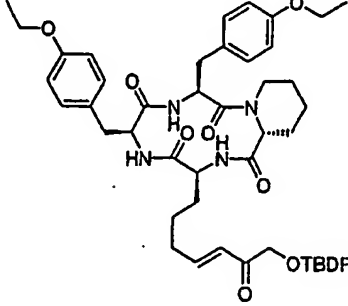
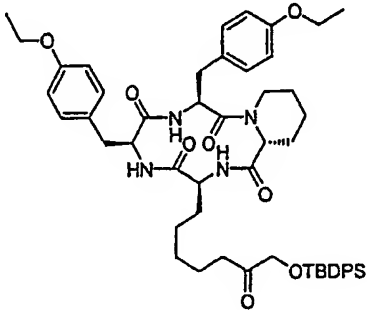
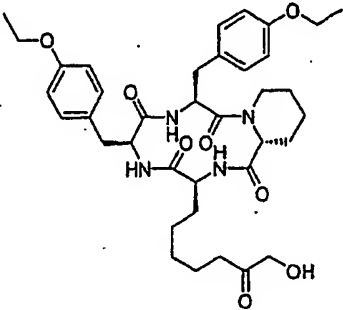
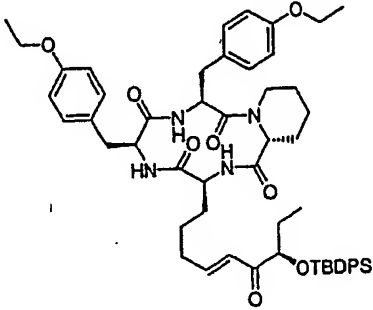
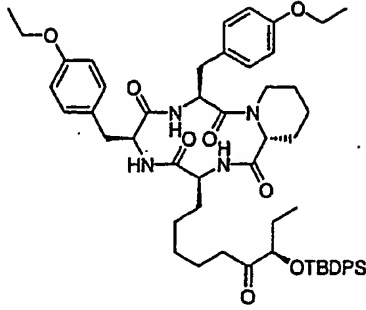
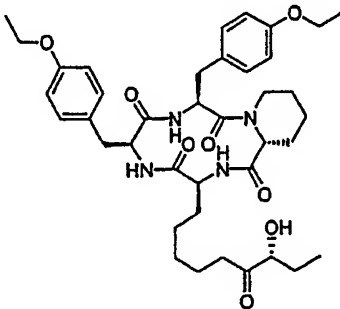
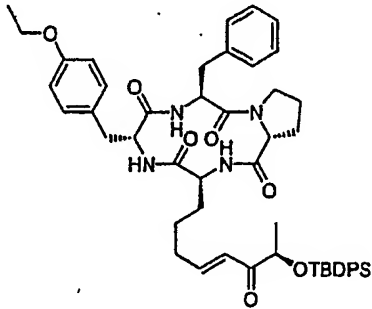
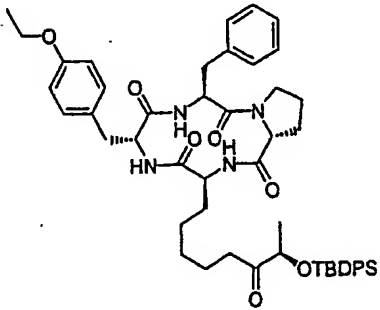
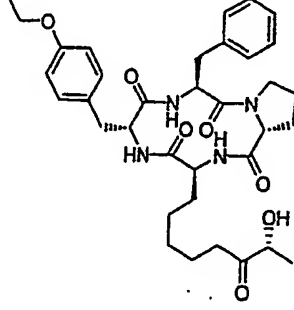
Compound E286	Compound E287
	
Compound E288	Compound E289
	
Compound E290	Compound E291
	
Compound E292	Compound E293
	

Table 2-107

Compound E294	Compound E295
	
Compound E296	Compound E297
	
Compound E298	Compound E299
	
Compound E300	Compound E301
	

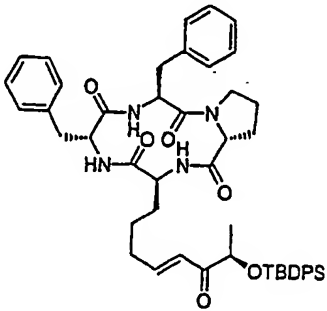
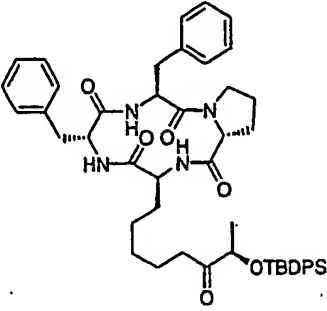
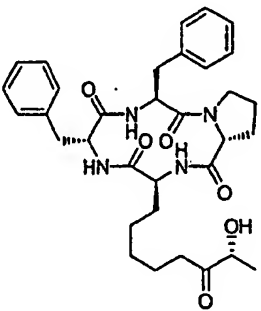
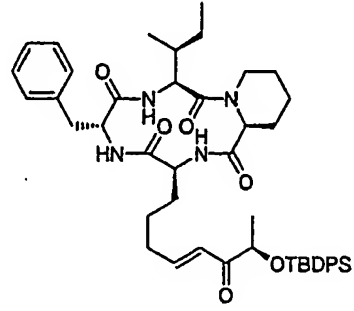
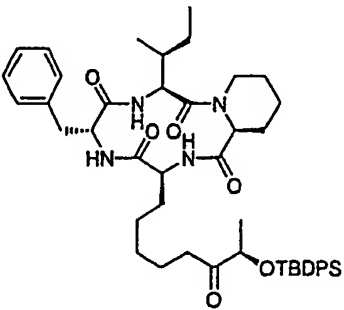
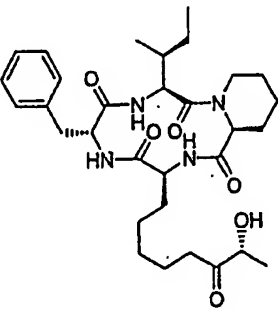
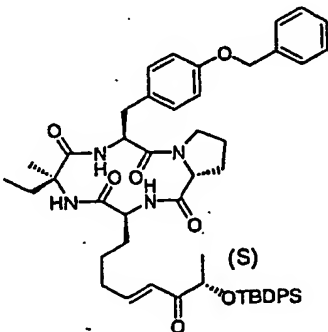
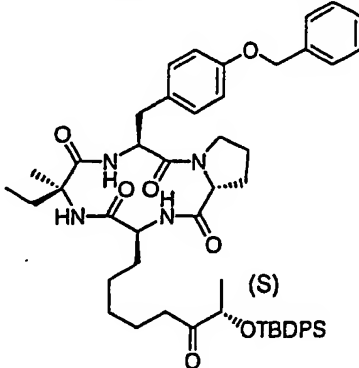
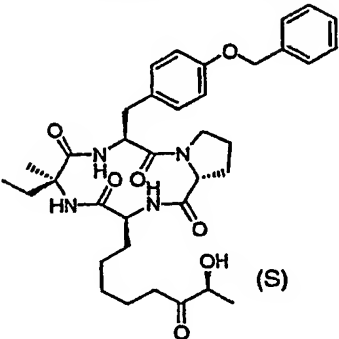
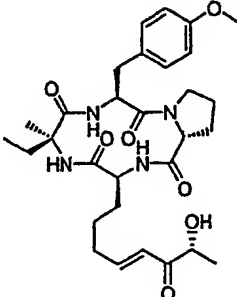
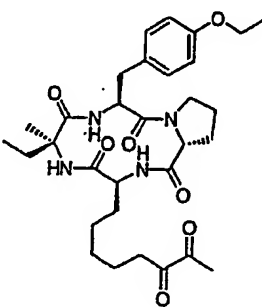
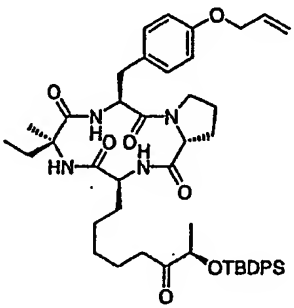
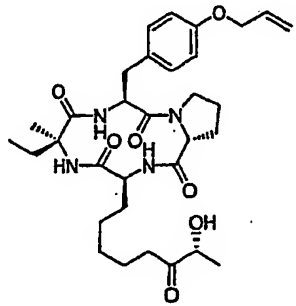
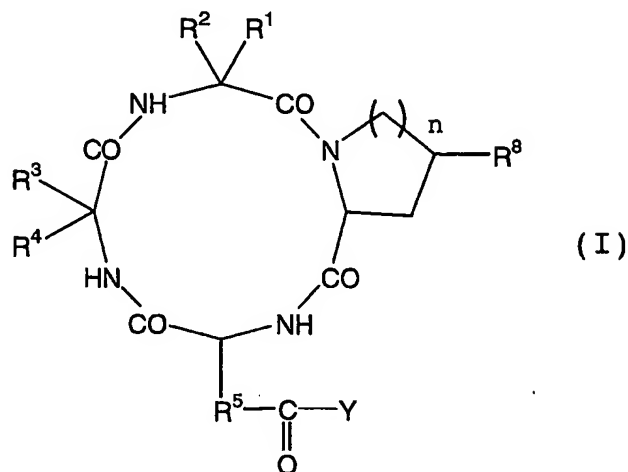
Compound E302	Compound E303
	
Compound E304	Compound E305
	
Compound E306	Compound E307
	
Compound E308	Compound E309
	

Table 2-109

Compound E310	Compound E311
	
Compound E312	Compound E313
	
Compound E314	
	

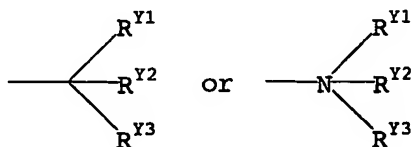
## CLAIMS

1. A cyclic tetrapeptide compound of the formula (I):



wherein

- 5 R<sup>1</sup> is hydrogen,  
 R<sup>2</sup> is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl or arylcarbamoyl(lower)alkyl,  
 10 R<sup>3</sup> and R<sup>4</sup> are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or  
 R<sup>3</sup> and R<sup>4</sup> are linked together to form lower alkylene or condensed ring, or  
 15 one of R<sup>3</sup> and R<sup>4</sup> is linked to the adjacent nitrogen atom to form a ring,  
 R<sup>5</sup> is lower alkylene or lower alkenylene,  
 Y is



- [wherein R<sup>Y1</sup> is hydrogen, halogen or optionally protected hydroxy,  
 20 R<sup>Y2</sup> is hydrogen, halogen, lower alkyl or phenyl, and  
 R<sup>Y3</sup> is hydrogen or lower alkyl],  
 R<sup>8</sup> is hydrogen or lower alkyl, and

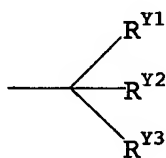
n is an integer of 1 or 2,

providing that,

when R<sup>3</sup> is methyl, R<sup>4</sup> is methyl or ethyl, R<sup>5</sup> is pentylene, R<sup>8</sup> is hydrogen,  
n is 1, R<sup>Y1</sup> is optionally substituted hydroxy, R<sup>Y2</sup> is methyl and R<sup>Y3</sup> is hydrogen,

- 5 then R<sup>2</sup> is not unsubstituted benzyl,  
or a salt thereof.

2. The cyclic tetrapeptide compound of claim 1, wherein  
R<sup>2</sup> is phenylcarbamoyl(lower)alkyl; lower alkylcarbamoyl(lower)alkyl; or  
10 phenyl(lower)alkyl optionally substituted with one or more suitable  
substituent(s) selected from the group consisting of lower alkyl,  
halo(lower)alkyl, lower alkoxy, ar(lower)alkoxy, cyano, hydroxy, halogen,  
amino, lower alkanoylamino, lower alkylsulfonylamino, aryl,  
cyclo(lower)alkyloxy, carboxy(lower)alkoxy, heterocyclic(lower)alkoxy,  
15 lower alkenyloxy, hydroxy(lower)alkyl, arylcarbamoyl,  
heterocycliccarbonyl, lower(alkyl)carbamoyl(lower)alkoxy,  
arylcarbamoyl(lower)alkoxy, lower(alkyl)carbamoyl(lower)alkyl,  
heterocyclic group, lower alkoxy carbonyl, lower  
alkoxy carbonyl(lower)alkoxy, lower alkylcarbamoyl,  
20 heterocycliccarbonyl(lower)alkyl, heterocycliccarbonyl(lower)alkoxy,  
aryl(lower)alkoxy and phenylcarbamoyl(lower)alkyl,  
R<sup>3</sup> is hydrogen or lower alkyl,  
R<sup>4</sup> is lower alkyl or phenyl(lower)alkyl substituted with lower alkoxy,  
R<sup>5</sup> is lower alkylene,  
25 Y is



[wherein R<sup>Y1</sup> is hydrogen or hydroxy, R<sup>Y2</sup> is halogen or lower alkyl and R<sup>Y3</sup>  
is hydrogen] and

R<sup>8</sup> is hydrogen or lower alkyl.

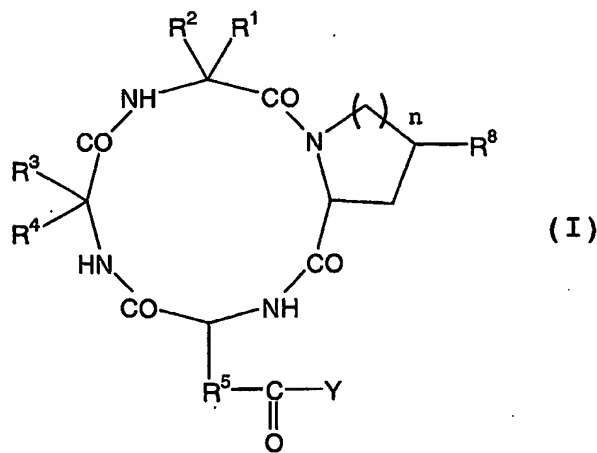
30

3. The cyclic tetrapeptide compound of claim 2, wherein  
R<sup>2</sup> is phenyl(lower)alkyl substituted with a substituent selected from the

- group consisting of lower alkyl, halo(lower)alkyl, lower alkoxy, phenyl(lower)alkyloxy, cyano, hydroxy, halogen, amino, lower alkanoylamino, (lower)alkylsulfonylamino, phenyl, cyclo(lower)alkyloxy, carboxy(lower)alkyloxy, pyridyl(lower)alkyloxy, lower alkenyloxy,
- 5 hydroxy(lower)alkyl, phenylcarbamoyl, piperidinocarbonyl, lower(alkyl)carbamoyl(lower)alkoxy, phenylcarbamoyl(lower)alkoxy, lower(alkyl)carbamoyl(lower)alkyl, pyridyl, lower alkoxycarbonyl, lower alkoxycarbonyl(lower)alkoxy, lower alkylcarbamoyl, morpholinocarbonyl(lower)alkyl, piperidinocarbonyl(lower)alkoxy,
- 10 phenyl(lower)alkoxy and phenylcarbamoyl(lower)alkyl,  $R^3$  is lower alkyl,  $R^4$  is lower alkyl, and  $R^5$  is lower alkylene.

- 15 4. A pharmaceutical composition containing the cyclic tetrapeptide compound of any of claims 1 to 3 as an active ingredient, in association with a pharmaceutically acceptable, substantially non-toxic carrier or excipient.
- 20 5. The cyclic tetrapeptide compound of any of claims 1 to 3 for use as a medicament.
6. A histone deacetylase inhibitor comprising a cyclic tetrapeptide compound of the formula (I):

25



wherein

R<sup>1</sup> is hydrogen,

R<sup>2</sup> is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl,

5 cyclo(lower)alkyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl or arylcarbamoyl(lower)alkyl,

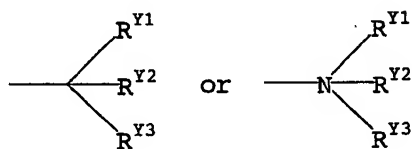
R<sup>3</sup> and R<sup>4</sup> are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s), heterocyclic(lower)alkyl optionally substituted with one or more suitable

10 substituent(s) or cyclo(lower)alkyl(lower)alkyl, or

R<sup>3</sup> and R<sup>4</sup> are linked together to form lower alkylene or condensed ring, or one of R<sup>3</sup> and R<sup>4</sup> is linked to the adjacent nitrogen atom to form a ring,

R<sup>5</sup> is lower alkylene or lower alkenylene,

Y is



15

[wherein R<sup>Y1</sup> is hydrogen, halogen, optionally protected hydroxy

R<sup>Y2</sup> is hydrogen, halogen, lower alkyl or phenyl, and

R<sup>Y3</sup> is hydrogen or lower alkyl],

R<sup>8</sup> is hydrogen or lower alkyl, and

20 n is an integer of 1 or 2,

providing that,

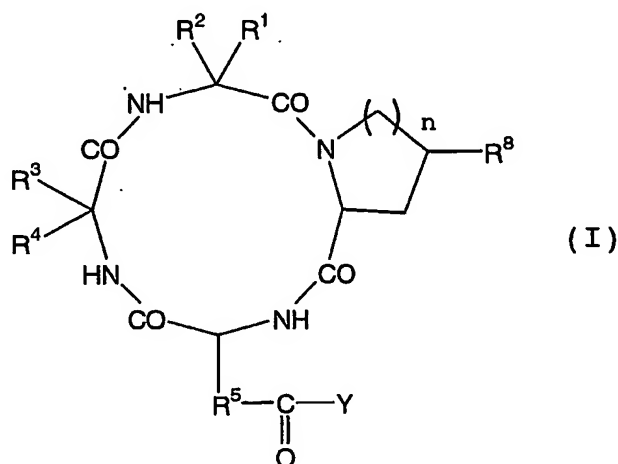
when R<sup>3</sup> is methyl, R<sup>4</sup> is methyl or ethyl, R<sup>5</sup> is pentylene, R<sup>Y1</sup> is optionally substituted hydroxy, R<sup>Y2</sup> is methyl and R<sup>Y3</sup> is hydrogen, then R<sup>2</sup> is not unsubstituted benzyl,

25 or a salt thereof.

7. A method for inhibiting histone deacetylase, comprising using a cyclic tetrapeptide compound (I) of claim 6.

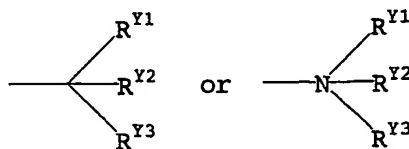
30 8. Use of a cyclic tetrapeptide compound (I) of claim 6 for the manufacture of a medicament for inhibiting histone deacetylase.

9. A pharmaceutical composition for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors, which  
 5 comprises, as an active ingredient, a cyclic tetrapeptide compound of the formula (I):



wherein

- $R^1$  is hydrogen,  
 $R^2$  is lower alkyl, aryl, ar(lower)alkyl optionally substituted with one  
 10 or more suitable substituent(s), heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbamoyl(lower)alkyl or arylcarbamoyl(lower)alkyl,  
 $R^3$  and  $R^4$  are each independently hydrogen, lower alkyl, ar(lower)alkyl optionally substituted with one or more suitable substituent(s),  
 15 heterocyclic(lower)alkyl optionally substituted with one or more suitable substituent(s) or cyclo(lower)alkyl(lower)alkyl, or  
 $R^3$  and  $R^4$  are linked together to form lower alkylene or condensed ring, or one of  $R^3$  and  $R^4$  is linked to the adjacent nitrogen atom to form a ring,  
 $R^5$  is lower alkylene or lower alkenylene,



20 Y is

[wherein  $R^{Y1}$  is hydrogen, halogen, optionally protected hydroxy  
 $R^{Y2}$  is hydrogen, halogen, lower alkyl or phenyl, and  
 $R^{Y3}$  is hydrogen or lower alkyl],  
 $R^8$  is hydrogen or lower alkyl, and

5 n is an integer of 1 or 2,

providing that,

when  $R^3$  is methyl,  $R^4$  is methyl or ethyl,  $R^5$  is pentylene,  $R^{Y1}$  is optionally substituted hydroxy,  $R^{Y2}$  is methyl and  $R^{Y3}$  is hydrogen, then  $R^2$  is not unsubstituted benzyl,

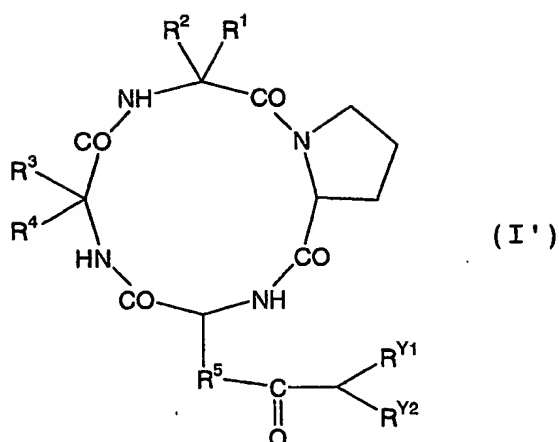
10 or a salt thereof.

10. A method for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections,  
15 autoimmune diseases, protozoal infections or tumors, which comprises administering an effective amount of the cyclic tetrapeptide compound (I) of claim 1 to a human being or an animal.

11. Use of the cyclic tetrapeptide compound (I) of claim 1 for the  
20 manufacture of a medicament for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.

25 12. A commercial package comprising the pharmaceutical composition of claim 9 and a written matter associated therewith, the written matter stating that the pharmaceutical composition may or should be used for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute  
30 promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.

13. A cyclic tetrapeptide compound of the formula (I'):



wherein

R<sup>1</sup> is hydrogen,

R<sup>2</sup> is ar(lower)alkyl optionally substituted with one or more suitable  
5 substituent(s),

R<sup>3</sup> and R<sup>4</sup> are each hydrogen or lower alkyl, or

R<sup>3</sup> and R<sup>4</sup> are linked together to form lower alkylene,

R<sup>5</sup> is lower alkylene or lower alkenylene,

R<sup>Y1</sup> is optionally protected hydroxy, and

10 R<sup>Y2</sup> is lower alkyl,

providing that,

when R<sup>3</sup> is methyl, R<sup>4</sup> is methyl or ethyl, R<sup>5</sup> is pentylene, R<sup>Y1</sup> is optionally  
substituted hydroxy and R<sup>Y2</sup> is methyl, then R<sup>2</sup> is not unsubstituted benzyl,  
or a salt thereof.

15

14. The cyclic tetrapeptide compound of claim 13, wherein

R<sup>2</sup> is phenyl(lower)alkyl optionally substituted with one or more suitable  
substituent(s) selected from the group consisting of lower alkoxy,  
ar(lower)alkyloxy, cyano, hydroxy and halogen,

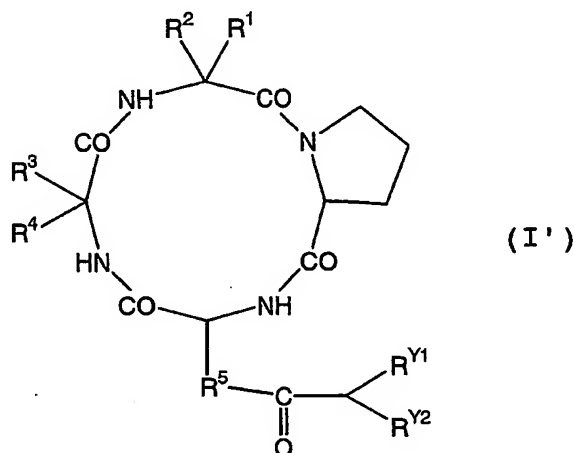
20 R<sup>3</sup> and R<sup>4</sup> are each lower alkyl, and

R<sup>5</sup> is lower alkylene.

15. A pharmaceutical composition containing the cyclic tetrapeptide  
compound of claim 13 or 14 as an active ingredient, in association with  
25 a pharmaceutically acceptable, substantially non-toxic carrier or  
excipient.

16. The cyclic tetrapeptide compound of claim 13 or 14 for use as a medicament.

- 5 17. A histone deacetylase inhibitor comprising a cyclic tetrapeptide compound of the formula (I'):



wherein

R<sup>1</sup> is hydrogen,

- 10 R<sup>2</sup> is ar(lower)alkyl optionally substituted with one or more suitable substituent(s),

R<sup>3</sup> and R<sup>4</sup> are each hydrogen or lower alkyl, or

R<sup>3</sup> and R<sup>4</sup> are linked together to form lower alkylene,

R<sup>5</sup> is lower alkylene or lower alkenylene,

R<sup>Y1</sup> is optionally protected hydroxy, and

- 15 R<sup>Y2</sup> is lower alkyl,

providing that,

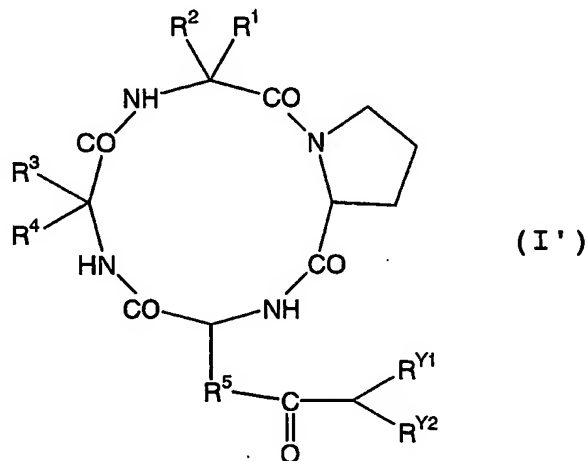
when R<sup>3</sup> is methyl, R<sup>4</sup> is methyl or ethyl, R<sup>5</sup> is pentylene, R<sup>Y1</sup> is optionally substituted hydroxy and R<sup>Y2</sup> is methyl, then R<sup>2</sup> is not unsubstituted benzyl, or a salt thereof.

20

18. A method for inhibiting histone deacetylase, comprising using a cyclic tetrapeptide compound (I') of claim 17.

19. Use of a cyclic tetrapeptide compound (I') of claim 17 for the  
25 manufacture of a medicament for inhibiting histone deacetylase.

20. A pharmaceutical composition for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors, which comprises, as an active ingredient, a cyclic tetrapeptide compound of the formula (I'):



wherein

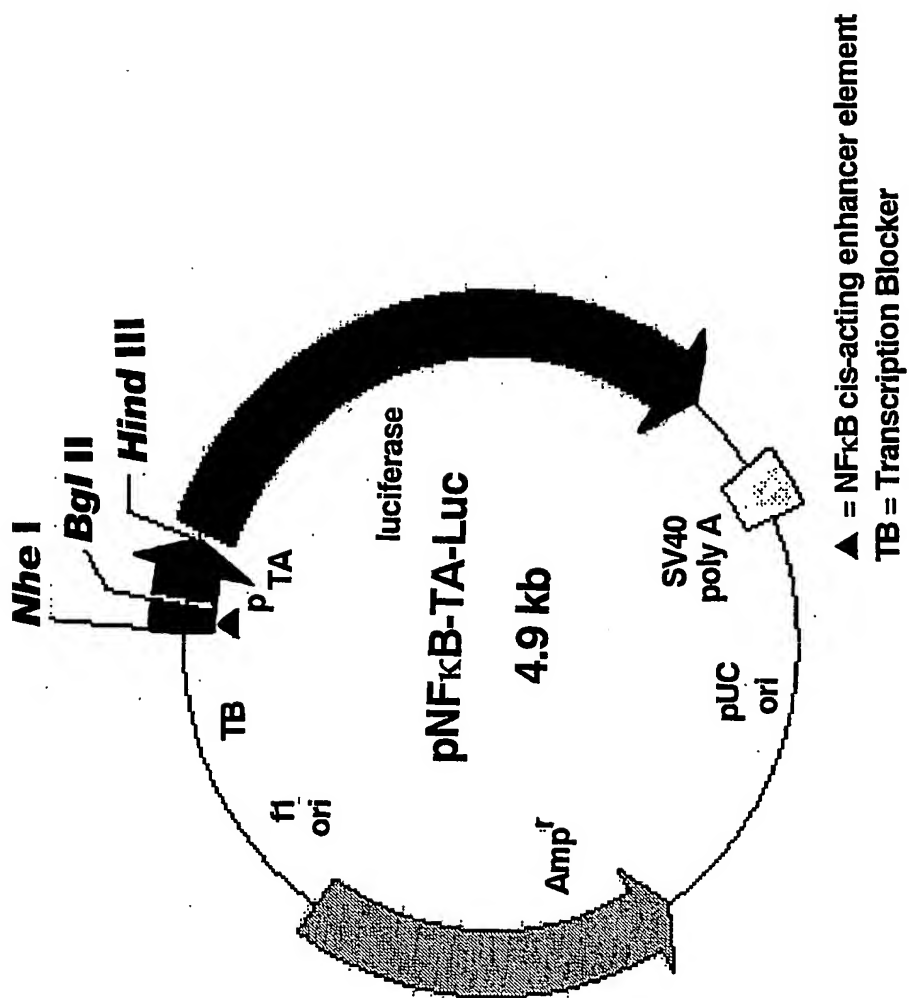
- R<sup>1</sup> is hydrogen,  
 10 R<sup>2</sup> is ar(lower)alkyl optionally substituted with one or more suitable substituent(s),  
 R<sup>3</sup> and R<sup>4</sup> are each hydrogen or lower alkyl, or  
 R<sup>3</sup> and R<sup>4</sup> are linked together to form lower alkylene,  
 R<sup>5</sup> is lower alkylene or lower alkenylene,  
 15 R<sup>Y1</sup> is optionally protected hydroxy, and  
 R<sup>Y2</sup> is lower alkyl,  
 providing that,  
 when R<sup>3</sup> is methyl, R<sup>4</sup> is methyl or ethyl, R<sup>5</sup> is pentylene, R<sup>Y1</sup> is optionally substituted hydroxy and R<sup>Y2</sup> is methyl, then R<sup>2</sup> is not unsubstituted benzyl,  
 20 or a salt thereof.

21. A method for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections,  
 25 autoimmune diseases, protozoal infections or tumors, which comprises

administering an effective amount of the cyclic tetrapeptide compound (I') of claim 13 to a human being or an animal.

22. Use of the cyclic tetrapeptide compound (I') of claim 13 for the manufacture of a medicament for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.

23. A commercial package comprising the pharmaceutical composition of claim 20 and a written matter associated therewith, the written matter stating that the pharmaceutical composition may or should be used for treating or preventing inflammatory disorders, diabetes, diabetic complications, homozygous thalassemia, fibrosis, cirrhosis, acute promyelocytic leukaemia (APL), organ transplant rejections, autoimmune diseases, protozoal infections or tumors.



**Fig. 1**

BEST AVAILABLE COPY

BEST AVAILABLE COPY

Effect on NF- $\kappa$ B activation in TNF  $\alpha$ -stimulated HEL cells (NF- $\kappa$ B reporter gene assay)

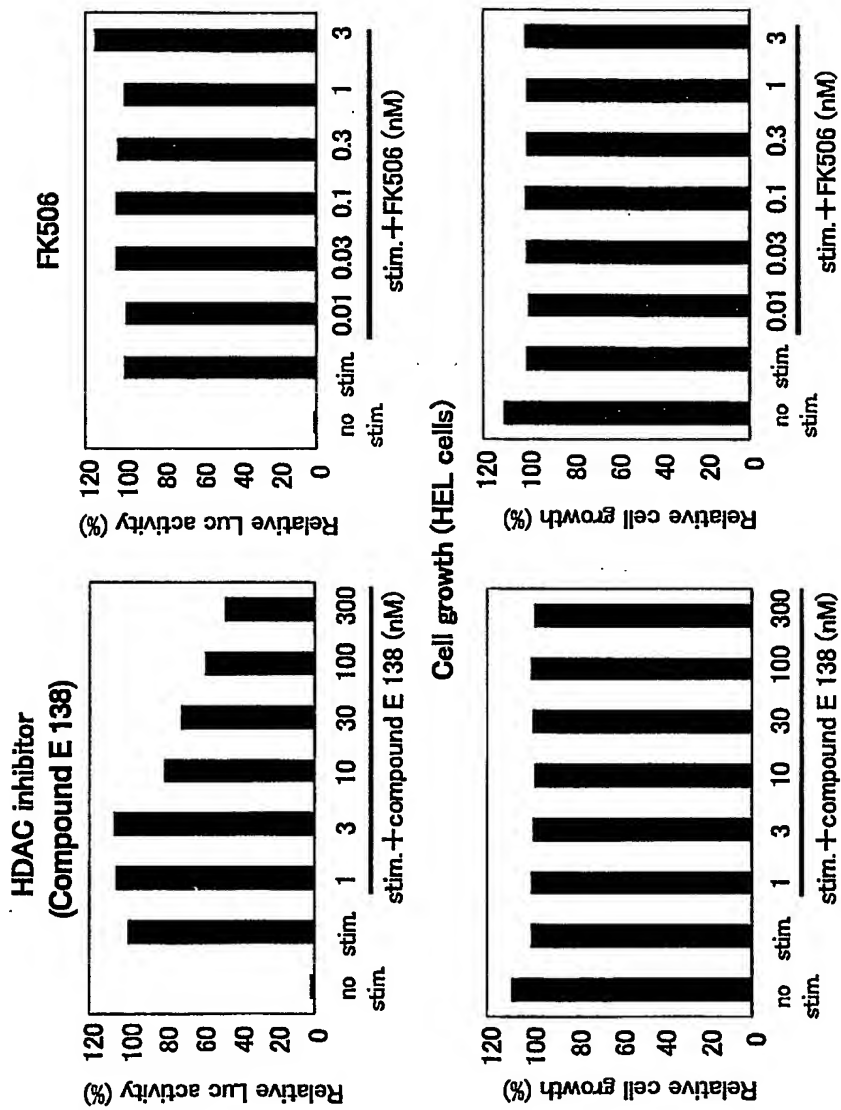
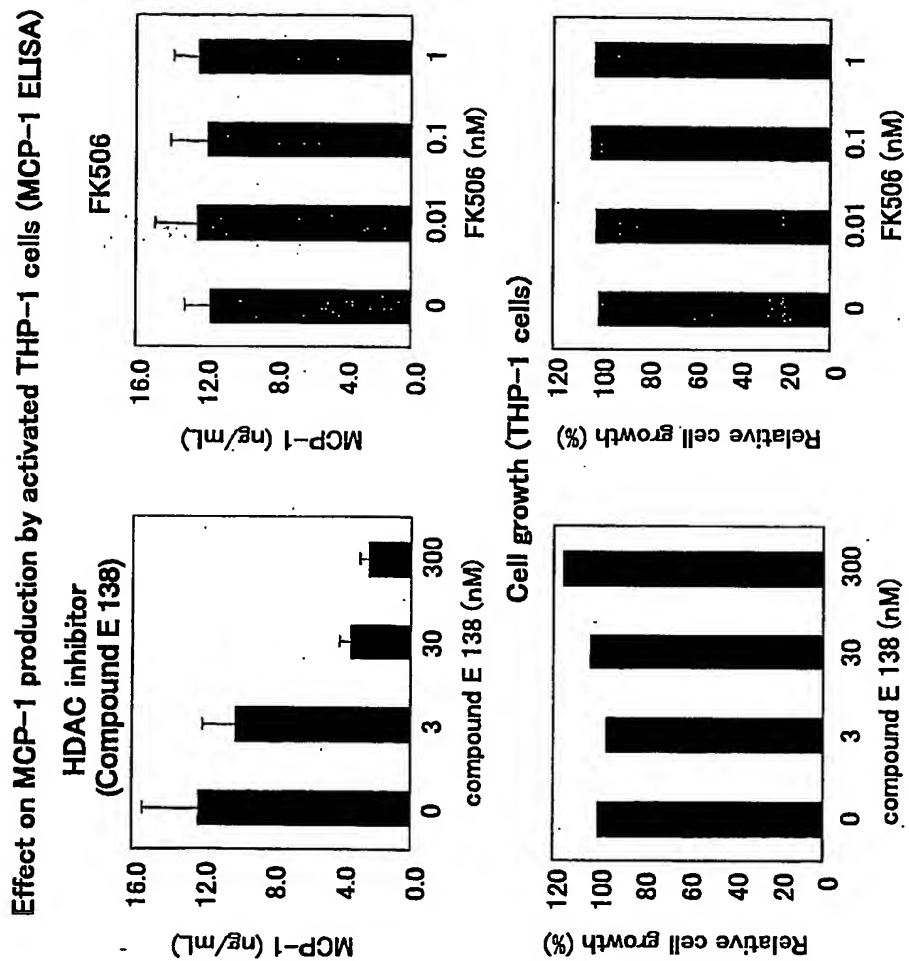


Fig. 2

BEST AVAILABLE COPY

**Fig. 3**

**THIS PAGE BLANK (USPTO**

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
17 July 2003 (17.07.2003)

PCT

(10) International Publication Number  
**WO 2003/057722 A3**

(51) International Patent Classification<sup>7</sup>: **C07K 5/12**,  
A61K 38/12, A61P 29/00, 35/00, 37/06

(21) International Application Number:  
PCT/JP2002/013754

(22) International Filing Date:  
27 December 2002 (27.12.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
PR 9779 28 December 2001 (28.12.2001) AU  
2002952117 10 October 2002 (10.10.2002) AU

(71) Applicant (for all designated States except US): **FUJISAWA PHARMACEUTICAL CO., LTD.** [JP/JP]; 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SATOH, Shigeki** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **URANO, Yasuharu** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **OSODA, Kazuhiko** [JP/JP]; c/o Fujisawa Pharmaceutical Co.,

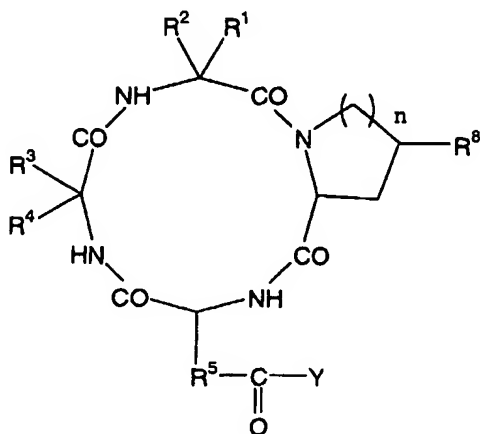
Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **HOSAKA, Mitsuru** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **SAWADA, Kozo** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **INOUE, Takayuki** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **MORI, Hiroaki** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **TAKAGAKI, Shoji** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **FUJIMURA, Takao** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **MATSUOKA, Hideaki** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP). **YOSHIZAWA, Katsuhiko** [JP/JP]; c/o Fujisawa Pharmaceutical Co., Ltd., 4-7, Doshomachi 3-chome, Chuo-ku, Osaka-shi, Osaka 541-8514 (JP).

(74) Agent: **TAKASHIMA, Hajime**; Fujimura Yamato Seimei Bldg., 2-14, Fushimimachi 4-chome, Chuo-ku, Osaka-shi, Osaka 541-0044 (JP).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,

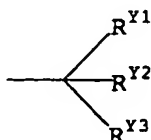
[Continued on next page]

(54) Title: CYCLIC TETRAPEPTIDE COMPOUND AND USE THEREOF

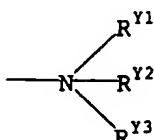


(I)

(57) Abstract: A cyclic tetrapeptide compound of the formula (I): wherein  $R_1$  is hydrogen;  $R_2$  is lower alkyl, aryl, optionally substituted ar(lower)alkyl, heterocyclic(lower)alkyl, cyclo(lower)alkyl(lower)alkyl, lower alkylcarbonyl(lower)alkyl or arylcarbonyl(lower)alkyl;  $R_3$  and  $R_4$  are each independently hydrogen, lower alkyl, optionally substituted ar(lower)alkyl, optionally substituted heterocyclic(lower)alkyl or cyclo(lower)alkyl(lower)alkyl, or  $R_3$  and  $R_4$  are linked together to form lower alkylene or condensed ring, or one of  $R_3$  and  $R_4$  is linked to the adjacent nitrogen atom to form a ring;  $R_5$  is lower alkylene or lower alkenylene, Y is [wherein  $R_{Y1}$  is hydrogen, halogen or optionally protected hydroxy,  $R_{Y2}$  is hydrogen, halogen, lower alkyl or phenyl, and  $R_{Y3}$  is hydrogen or lower alkyl];  $R_6$  is hydrogen or lower alkyl; and n is an integer of 1 or 2, or a salt thereof.



(II)



(III)



CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— with international search report

**(88) Date of publication of the international search report:**

22 April 2004

**(84) Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK,

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 02/13754

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K5/12 A61K38/12 A61P29/00 A61P35/00 A61P37/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 21979 A (HINO MOTOHIRO ;MORI HIROAKI (JP); FUJISAWA PHARMACEUTICAL CO (JP);) 20 April 2000 (2000-04-20) p. 1, l. 25; p. 2, l. 10-13; p. 7, l. 25, 28; p. 24, l. 25-p. 29, l. 7 ---	1-11, 13-22
X	WO 00 08048 A (ABE FUMIE ;HINO MOTOHIRO (JP); MORI HIROAKI (JP); YOSHIMURA SEIJI) 17 February 2000 (2000-02-17) page 1, line 33,34 page 6, line 10-15 ---	1-11, 13-22
X	EP 1 010 705 A (JAPAN ENERGY CORP) 21 June 2000 (2000-06-21) p. 3, l. 27-29 & compounds X-XXI; XXIII-XXXXIII --- -/--	1-11, 13-22



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

1 August 2003

Date of mailing of the international search report

12.12.03

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Lopez García, F

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/JP 02/13754

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01 07042 A (COLLETTI STEVEN L ; WYVRATT MATTHEW J (US); GURNETT ANNE M (US); ME) 1 February 2001 (2001-02-01) p. 1, l. 7-9 & examples 4a; 20b; 21b; 22b; 23b; 27; 29; 30; 32; 33; 52b; 53; 55a; 68-100; 102-110; 120-125; 127-132; 145-147; 152-157; 163; 164; 169; 170 -----	1-11, 13-22
X	GB 2 309 696 A (MERCK & CO INC) 6 August 1997 (1997-08-06) p. 2, l. 30-31 & p.6, l. 5-p. 7, l. 7. -----	1-11, 13-22

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/JP 02/13754

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 12 and 23  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1, 4-11 (partially); 2, 3, 13-22 (completely)

Compounds of formula I, wherein  $n=1$  and Y is  $-C(RY1)(RY2)(RY3)$ , their compositions and use

2. Claims: 1, 4-11 (partially); 2, 3 (completely)

Compounds of formula I, wherein  $n=2$  and Y is  $-C(RY1)(RY2)(RY3)$ , their compositions and use

3. Claims: 1, 4-11 (partially)

Compounds of formula I, wherein  $n=1$ ,  $R8=H$  and Y is  $-N(RY1)(RY2)(RY3)$ , their compositions and use

4. Claims: 1, 4-11 (partially)

Compounds of formula I, wherein  $n=2$ ,  $R8=H$  and Y is  $-N(RY1)(RY2)(RY3)$ , their compositions and use

5. Claims: 1, 4-11 (partially)

Compounds of formula I, wherein  $n=1$  or  $2$ , Y is  $-N(RY1)(RY2)(RY3)$  and  $R8$  is different from H, their compositions and use

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 7, 10, 18 and 21 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

-----

Continuation of Box I.1

Claims Nos.: 12 and 23

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy  
Rule 39.1(v) PCT - Presentation of information

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 02/13754

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0021979	A	20-04-2000	AU 6007299 A	01-05-2000
			BR 9914779 A	03-07-2001
			CA 2346943 A1	20-04-2000
			CN 1330660 T	09-01-2002
			CZ 20011342 A3	12-09-2001
			EP 1123309 A2	16-08-2001
			HU 0103985 A2	28-02-2002
			WO 0021979 A2	20-04-2000
			JP 2002527449 T	27-08-2002
			PL 348648 A1	03-06-2002
			TR 200101049 T2	21-01-2002
WO 0008048	A	17-02-2000	WO 0008048 A2	17-02-2000
EP 1010705	A	21-06-2000	AU 732299 B2	12-04-2001
			AU 8888598 A	22-03-1999
			CA 2302451 A1	11-03-1999
			EP 1010705 A1	21-06-2000
			NO 20001045 A	27-04-2000
			NZ 503061 A	31-08-2001
			US 6399568 B1	04-06-2002
			WO 9911659 A1	11-03-1999
			ZA 9808023 A	02-03-1999
WO 0107042	A	01-02-2001	AU 6109600 A	13-02-2001
			CA 2378849 A1	01-02-2001
			EP 1204411 A1	15-05-2002
			JP 2003505417 T	12-02-2003
			WO 0107042 A1	01-02-2001
			US 2003078369 A1	24-04-2003
GB 2309696	A	06-08-1997	US 5922837 A	13-07-1999